Optimisation de la CEC: vers une CEC biocompatible

Réduction ciblée d'anticoagulation

(Reduced Goal Directed Anticoagulation)

Pr Christophe Baufreton, CHU Angers
Cours du DU de CEC (Bordeaux), 27 février 2026

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CEC et anticoagulation conventionnelle

- Préparation
  - → Circuit de CEC débullé
  - → Dose héparine IV: 300 UI/Kg (par le chirurgien dans l'OD)
  - → 5000 UI dans liquide d'amorçage
  - → Check-list
- Anticoagulation: ACT > 480s
- Monitorage: Hémochron™ ou HMS™
- Neutralisation: Protamine dose pour dose
- **Suivi morbidité immédiate**
  - → **Saignement (± reprise au bloc)**
  - → **Transfusion**

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CEC optimale ?

Anesthesia & Analgesia

Optimal Perfusion During Cardiopulmonary Bypass: An Evidence-Based Approach

Glenn S. Murphy, MD*
Eugene A. Hessel II, MD†
Robert C. Groom, MS, CCP‡

In this review, we summarize the best available evidence to guide the conduct of adult cardiopulmonary bypass (CPB) to achieve "optimal" perfusion. At the present time, there is considerable controversy relating to appropriate management of physiologic variables during CPB. Low-risk patients tolerate mean arterial blood pressures of 50–60 mm Hg without apparent complications, although limited data suggest that higher-risk patients may benefit from mean arterial blood pressures >70 mm Hg. The optimal hematocrit on CPB has not been defined, with large data-based investigations demonstrating that both severe hemodilution and transfusion of packed red blood cells increase the risk of adverse postoperative outcomes. Oxygen delivery is determined by the pump flow rate and the arterial oxygen content and organ injury may be prevented during more severe hemodilutional anemia by increasing pump flow rates. Furthermore, the optimal temperature during CPB likely varies with physiologic goals, and recent data suggest that aggressive rewarming practices may contribute to neurologic injury. The design of components of the CPB circuit may also influence tissue perfusion and outcomes. Although there are theoretical advantages to centrifugal blood pumps over roller pumps, it has been difficult to demonstrate that the use of centrifugal pumps improves clinical outcomes. Heparin coating of the CPB circuit may attenuate inflammatory and coagulation pathways, but has not been clearly demonstrated to reduce major morbidity and mortality. Similarly, no distinct clinical benefits have been observed when open venous reservoirs have been compared to closed systems. In conclusion, there are currently limited data upon which to confidently make strong recommendations regarding how to conduct optimal CPB. There is a critical need for randomized trials assessing clinically significant outcomes, particularly in high-risk patients.
(Anesth Analg 2009;108:1394–417)

Total cardiopulmonary bypass (CPB) has been used for cardiac surgery for over half a century and is used successfully thousands of times each day worldwide. Although most patients tolerate the procedure reasonably well, subtle as well as clinically apparent evidence of its harm are often encountered (e.g., excessive bleeding, systemic inflammation, strokes and neuropsychological dysfunction, renal, pulmonary, and cardiac dysfunction and multiorgan failure). The techniques for conducting CPB were developed based upon physiologic principles using materials which were available at that time, followed by animal testing and eventually clinical trials.[1,2] Over the past five decades, numerous advancements in equipment and techniques have been introduced with notable improvements in morbidity and mortality.

Although some of these changes have been introduced based upon logical principles, laboratory investigations and clinical studies, more often, these changes have been driven by the personal biases, clinical impressions, experiences of individual cardiac surgical groups, and industry pressures. This has resulted in major differences in practice among teams conducting CPB.[3]

A new paradigm of medical practice, evidence-based medicine, has emerged which encourages clinical practice based upon objective clinical evidence. This paradigm posits that there is a hierarchy of strength or quality of evidence and that practice should be guided by the highest level of available

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Robert Groom has received research grants or equipment from the Sorin Group, Somanetics Corporation, Spencer Technology, And Terumo Cardiovascular.

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DOI: 10.1213/ane.0b013e3181875e2e

- Management des variables physiologiques et des composants de la machine cœur-poumon
- **Mais rien sur la gestion de l'anticoagulation !**

Murphy GS, Hessel EA, Groom RC. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. Anesth Analg. 2009;108(5):1394–417.

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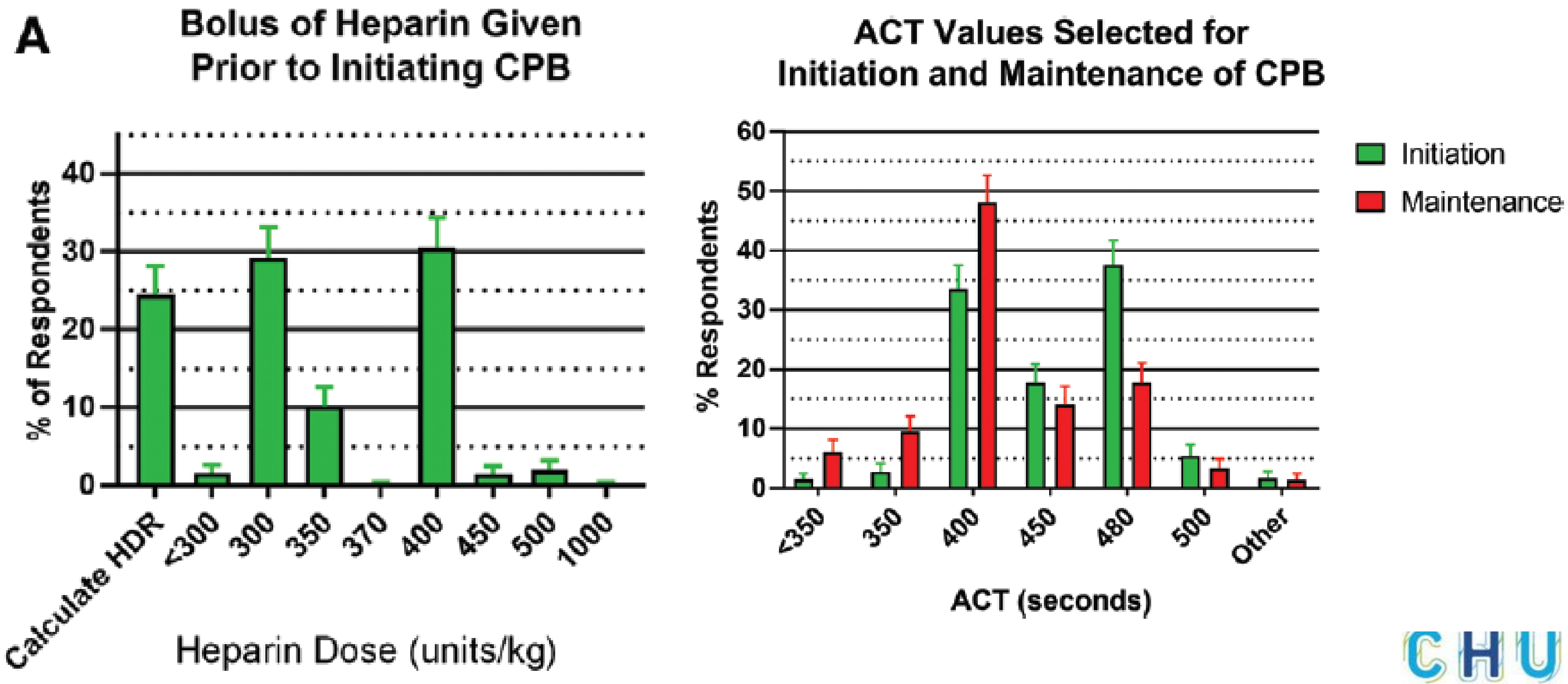
Gestion dans le monde de l'anticoagulation en CEC en 2018

For those respondents who used an activated clotting time to determine adequate anticoagulation for CPB initiation, an activated clotting time value of 480 or 400 seconds was used by 70.7%



Sniecinski RM, Bennett-Guerrero E, Shore-Lesserson L. Anticoagulation Management and Heparin Resistance During Cardiopulmonary Bypass. Anesth Analg. 2018 Dec;:1.

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Sur quoi reposent les recommandations pour l'anticoagulation en CEC ?
Faiblesse du niveau de preuve pour le gold-standard !

Heparin therapy during extracorporeal circulation

I. Problems inherent in existing heparin protocols

Five heparin protocols, representative of about 30 presently used throughout the country, were analyzed. T… …sion of protamine neutralization at … …died. In each of 50 patients, the half … …easured. Knowledge of the patient's age, … …dicting heparin kinetics. The stud… …and the 2 patients with the shortest hepa… …e greatest sensitivity to heparin and the 2 who showed the least. By computer simulation, each was managed according to the five protocols and by a monitoring procedure. The protocols failed to provide safe anticoagulation or precise protamine neutralization, whereas the simplified monitoring approach was uniformly successful.

8 patients
Computer simulation

Brian S. Bull, M.D.,* Ralph A. Korpman, M.D.,* Wilfred M. Huse, M.D.,** and Bernard D. Briggs, M.D.,*** *Loma Linda, Calif.*

Heparin therapy during extracorporeal circulation

II. The use of a dose-response curve to individualize heparin and protamine dosage

Because the administration of he… …to a set protocol will fail to anticoagulate safely or neutra… …number of patients, a method of monitoring heparin t… …bypass is presented. A dose response curve relating heparin dosage to its effect on the activated coagulation time (ACT) can be determined with sufficient accuracy for clinical purposes from three ACT's. Preparation of such a curve makes it possible to maintain anticoagulation in a safe range during bypass and minimizes the number of monitoring tests of coagulation required. At the conclusion of bypass, this curve can be used to predict the precise amount of protamine needed for neutralization. Freed from the confusing effects of hyperhepurinemia or protamine excess, the physician can diagnose and treat postoperative bleeding problems much more readily.

25 patients

Brian S. Bull, M.D.,* Wilfred M. Huse, M.D.,** Floyd S. Brauer, M.D.,*** and Ralph A. Korpman, M.D.,* *Loma Linda, Calif.*

According to Bull (1975) ACT value:

- < *180 seconds: life threatening*
- *180-300 seconds: questionable*
- > *300 seconds: safe*
- > *600 seconds: unwise*

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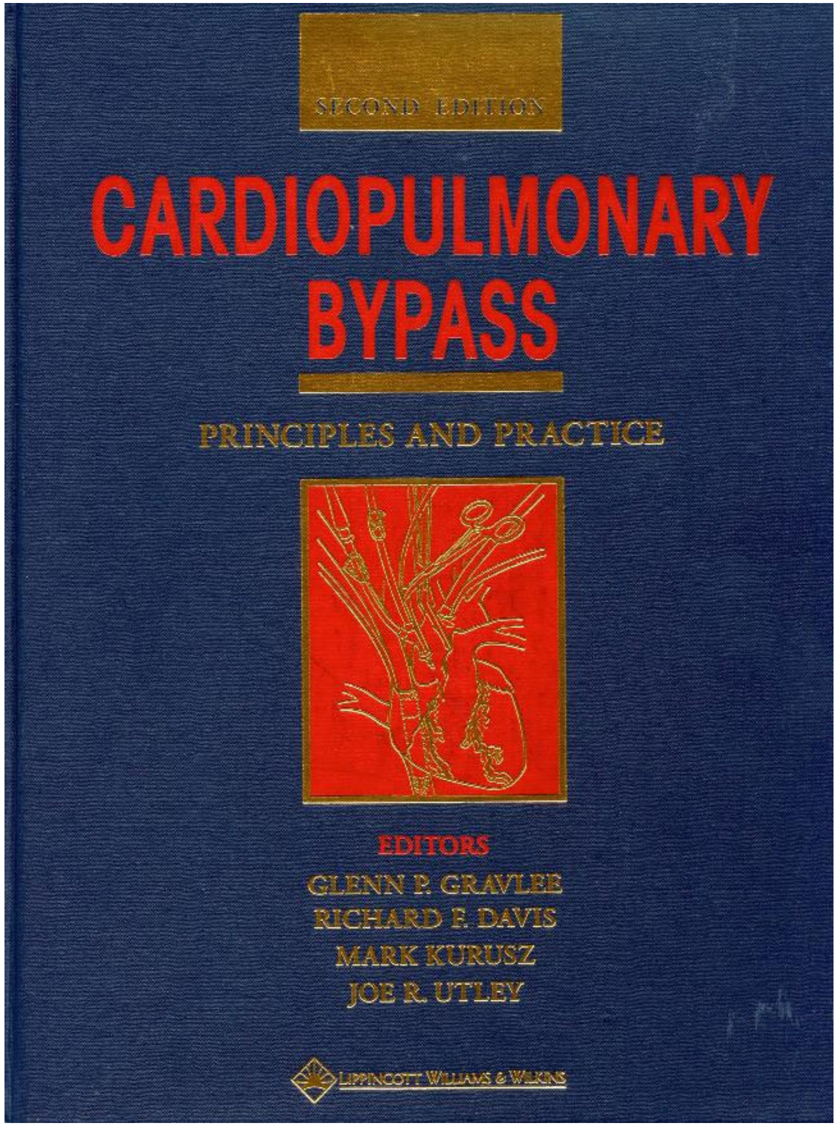
Que peut-on lire dans les ouvrages de référence ?



Bull et al. also recommended attaining an ACT of 480 seconds before initiating CPB, suggesting that this particular ACT value provides a safety margin over the believed minimum safe ACT of 300 seconds.

It appears that many practitioners have misinterpreted *their recommendation by assuming that an ACT of 480 seconds represents the minimum safe level for CPB anticoagulation, when the authors were simply offering* ***a suggestion without scientific validation***

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EDITORIAL

EDITORIAL

Patient blood management during cardiac surgery: Do we have enough evidence for clinical practice?

Factor	Limitations of current evidence	Issues for future research
Anticoagulation measurement	Optimal measure and threshold unclear	Which is the optimal method with which to monitor anticoagulation? What are the minimum acceptable target threshold levels?
Reduced systemic heparinization	Heparin dose and target ACT not clearly defined; lack of high-level evidence	Does reduction of systemic heparinization in the setting of biocompatible circuits decrease bleeding and transfusion rate?

Ranucci M, Aronson S, Dietrich W, Dyke CM, Hofmann A, Karkouti K, et al. Patient blood management during cardiac surgery: do we have enough evidence for clinical practice? J Thorac Cardiovasc Surg. Elsevier; 2011 Aug;142(2):249.e1-32.

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Guidelines US 2018 pour l'anticoagulation en CEC

CLINICAL PRACTICE GUIDELINES

The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: Clinical Practice Guidelines*—Anticoagulation During Cardiopulmonary Bypass

Linda Shore-Lesserson, MD, Robert A. Baker, PhD, CCP, Victor A. Ferraris, MD, PhD, Philip E. Greilich, MD, David Fitzgerald, MPH, CCP, Philip Roman, MD, MPH, and John W. Hammon, MD

Department of Anesthesiology, Zucker School of Medicine at Hofstra Northwell, Hempstead, New York; Cardiac Surgery Research and Perfusion, Flinders University and Flinders Medical Center, Adelaide, South Australia, Australia; Division of Cardiovascular and Thoracic Surgery, University of Kentucky, Lexington, Kentucky; Department of Anesthesiology and Pain Management, University of Texas-Southwestern Medical Center, Dallas, Texas; Division of Cardiovascular Perfusion, Medical University of South Carolina, Charleston, South Carolina; Department of Anesthesiology, Saint Anthony Hospital, Lakewood, Colorado; and Department of Cardiothoracic Surgery, Wake Forest University School of Medicine, Winston-Salem, North Carolina

Despite more than a half century of "safe" cardiopulmonary bypass (CPB), the evidence base surrounding the conduct of anticoagulation therapy for CPB has not been organized into a succinct guideline. For this and other reasons, there is enormous practice variability relating to the use and dosing of heparin, monitoring heparin anticoagulation, reversal of anticoagulation, and the use of alternative anticoagulants. To address this and other gaps, The Society of Thoracic Surgeons, the Society of Cardiovascular Anesthesiologists, and the American Society of Extracorporeal Technology developed an Evidence Based Workgroup. This was a group of interdisciplinary professionals gathered to summarize the evidence and create practice recommendations for various aspects of CPB. To date, anticoagulation practices in CPB have not been standardized in accordance with the evidence base. This clinical practice guideline was written with the intent to fill the evidence gap and to establish best practices in anticoagulation therapy for CPB using the available evidence.

To identify relevant evidence, a systematic review was outlined and literature searches were conducted in PubMed using standardized medical subject heading (MeSH) terms from the National Library of Medicine list of search terms. Search dates were inclusive of January 2000 to December 2015. The search yielded 833 abstracts, which were reviewed by two independent reviewers. Once accepted into the full manuscript review stage, two members of the writing group evaluated each of 286 full papers for inclusion eligibility into the guideline document. Ninety-six manuscripts were included in the final review. In addition, 17 manuscripts published before 2000 were included to provide method, context, or additional supporting evidence for the recommendations as these papers were considered sentinel publications.

Members of the writing group wrote and developed recommendations based on review of the articles obtained and achieved more than two thirds agreement on each recommendation. The quality of information for a given recommendation allowed assessment of the level of evidence as recommended by the American College of Cardiology Foundation/American Heart Association Task

*These clinical practice guidelines (CPGs) were developed prior to the publication of "The American Association for Thoracic Surgery/Society of Thoracic Surgeons Position Statement on Developing Clinical Practice Documents" (Bakaeen, et al. Ann Thorac Surg 2017;103:1350–6), and thus their development did not strictly adhere to the process for CPGs outlined in that document. Nevertheless, these CPGs were the product of a lengthy and rigorous review by a multidisciplinary panel of experts, and approved by all three participating societies. All future STS CPGs appearing in *The Annals of Thoracic Surgery* will be developed in accordance to the aforementioned Position Statement.

This article is copublished in *The Annals of Thoracic Surgery*, *Anesthesia & Analgesia*, and the *Journal of ExtraCorporeal Technology*.

The Society of Thoracic Surgeons requests that this document be cited as follows: Shore-Lesserson L, Baker RA, Ferraris VA, Greilich PE, Fitzgerald D, Roman P, Hammon JW. The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: clinical practice guidelines—anticoagulation during cardiopulmonary bypass. Ann Thorac Surg 2018;105:650–62.

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The Appendix and Supplemental Tables can be viewed in the online version of this article [https://doi.org/10.1016/j.athoracsur.2017.09.061] on http://www.annalsthoracicsurgery.org.

0003-4975/$36.00
https://doi.org/10.1016/j.athoracsur.2017.09.061

REPORT

It is reasonable to maintain activated clotting time above 480 seconds during CPB. However, this minimum threshold value is an approximation and may vary based on the bias of the instrument being used (Level of Evidence C)

To maintain a margin of safety above 400 seconds, the minimum acceptable ACT value of approximately 480 seconds became a "standard of care" that was used in numerous future studies and in clinical practice, but was ***based on limited evidence***

Options for calculating the initial heparin bolus include a fixed, weight-based dose, (eg, 300 IU/kg), or use of point-of-care tests that measure the whole blood sensitivity to heparin using an associated dose response.

Depuis 1975 les patients ont changé !

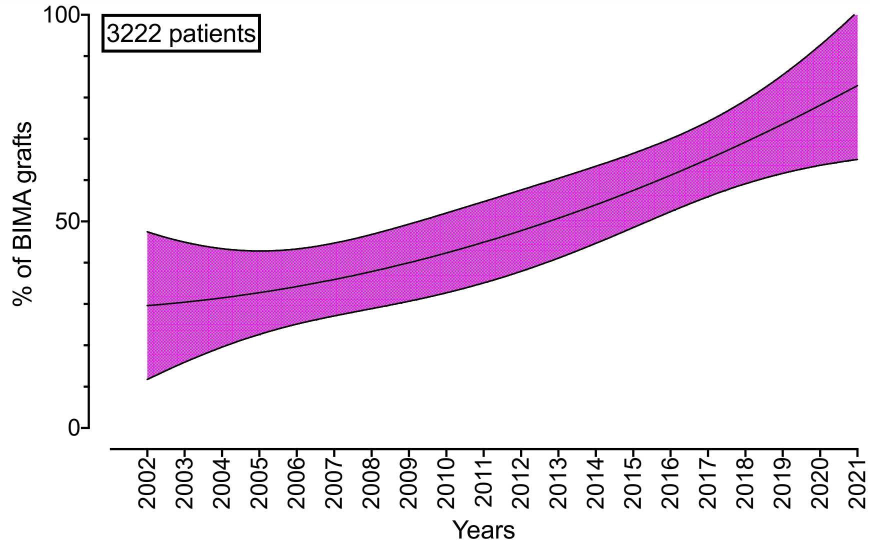
Changing Volumes, Risk Profiles, and Outcomes of Coronary Artery Bypass Grafting and Percutaneous Coronary Interventions

Gabriel S. Aldea, MD, Nahush A. Mokadam, MD, Rayland Melford, Jr, MD, Douglas Stewart, MD, Charles Maynard, PhD, Mark Reisman, MD, and Richard Goss, MD, MPH

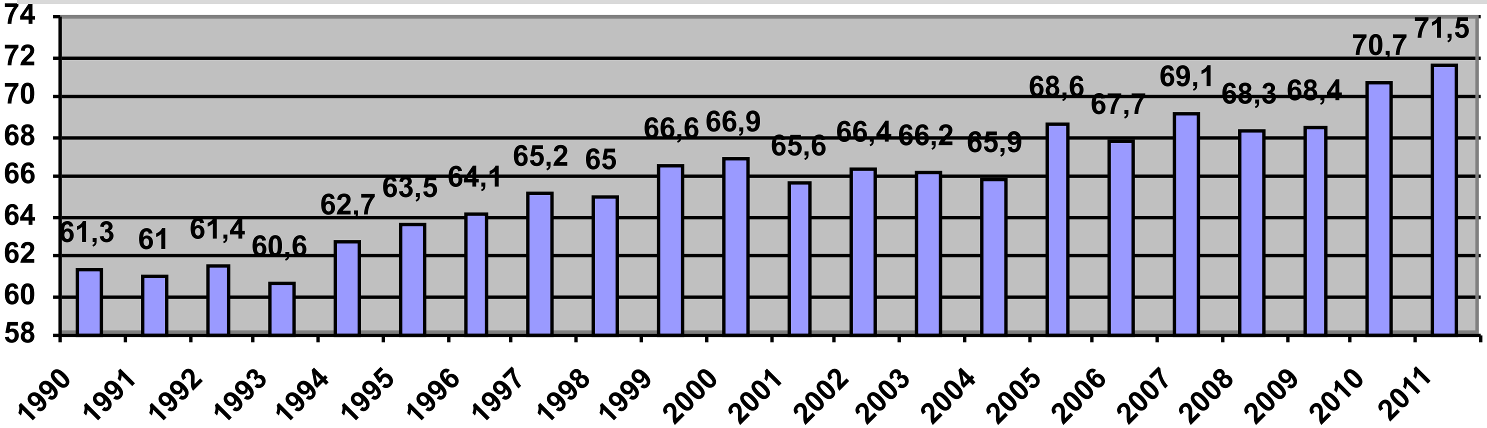
Fifteen-Year Outcome Trends for Valve Surgery in North America

Richard Lee, MD, Shuang Li, MS, J. Scott Rankin, MD, Sean M. O'Brien, PhD, James S. Gammie, MD, Eric D. Peterson, MD, Patrick M. McCarthy, MD, and Fred H. Edwards, MD, for The Society of Thoracic Surgeons Adult Cardiac Surgical Database

Aldea GS, et al. Ann Thorac Surg. 2009 Jun 1;87(6):1828-38.
Lee R, et al. Ann Thorac Surg. 2011 Mar 1;91(3):677-84.



Evolution de l'âge des patients et des modes de revascularization sur 20 ans au CHU d'Angers



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Impact de la double anti-aggrégation plaquettaire sur le saignement post-opératoire

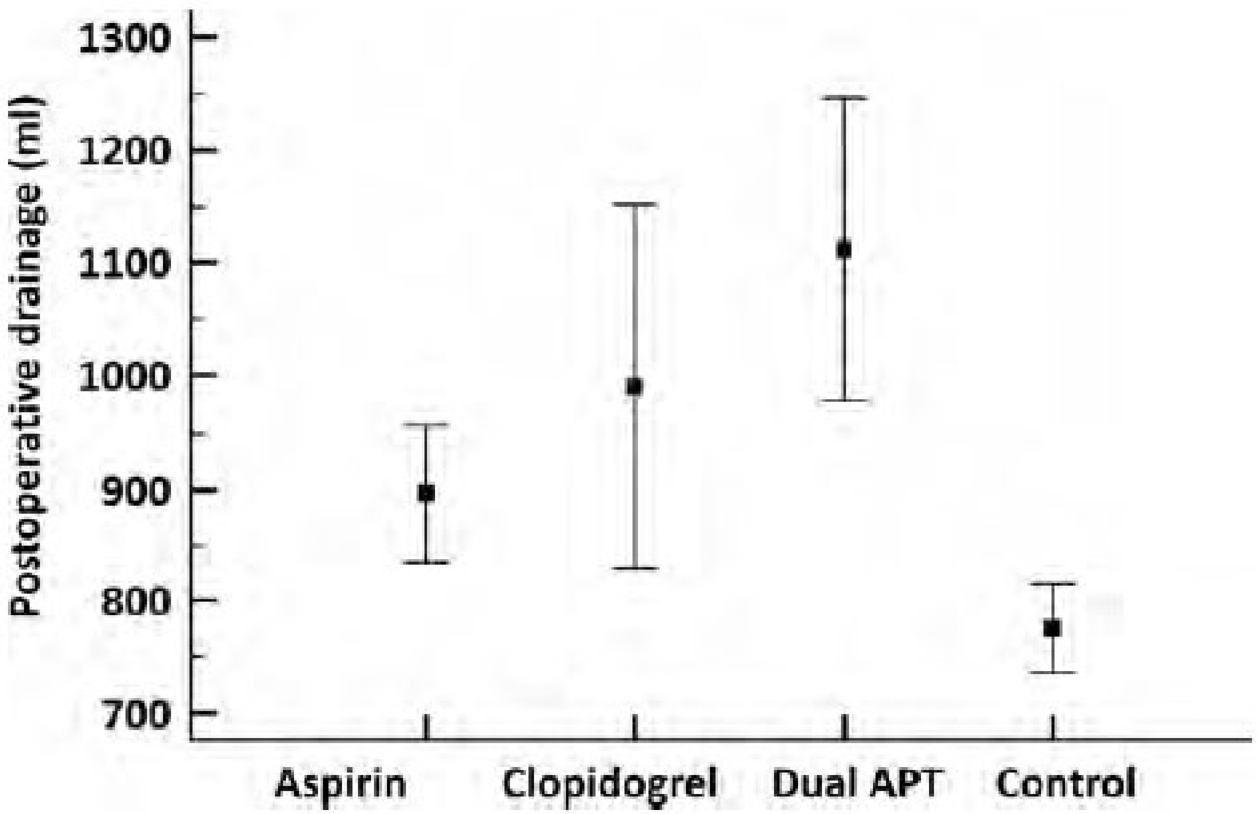

Figure 3: Postoperative chest tube drainage volumes, by antiplatelet treatment (mean and 95% CI). Matched patients.

Kremke M, et al. Antiplatelet therapy at the time of coronary artery bypass grafting: a multicentre cohort study. Eur J Cardiothorac Surg. 2013 Jul 11;44(2):e133-40.

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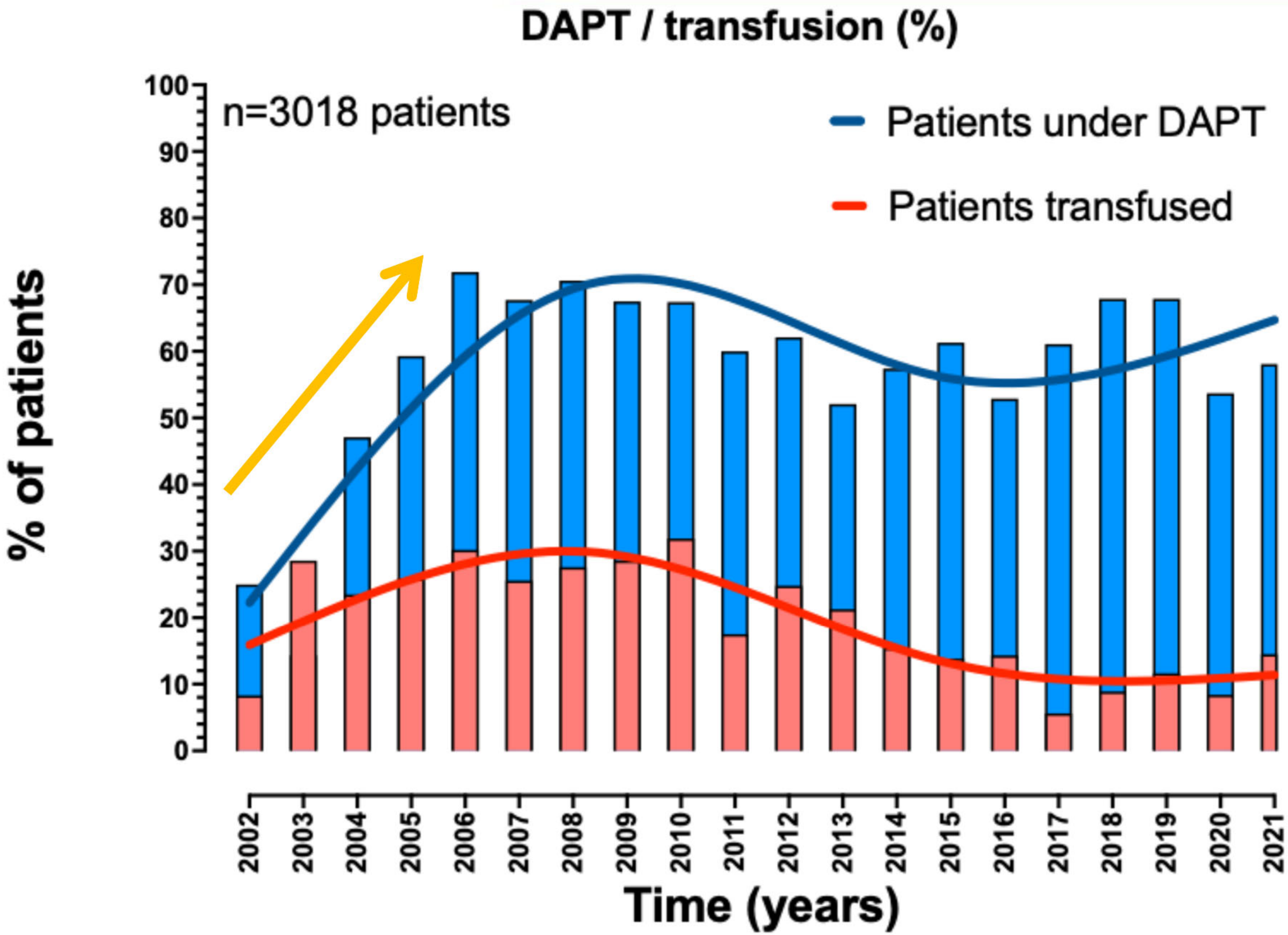
Impact de la double anti-aggrégation plaquettaire sur la transfusion post-opératoire (Angers)



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2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery

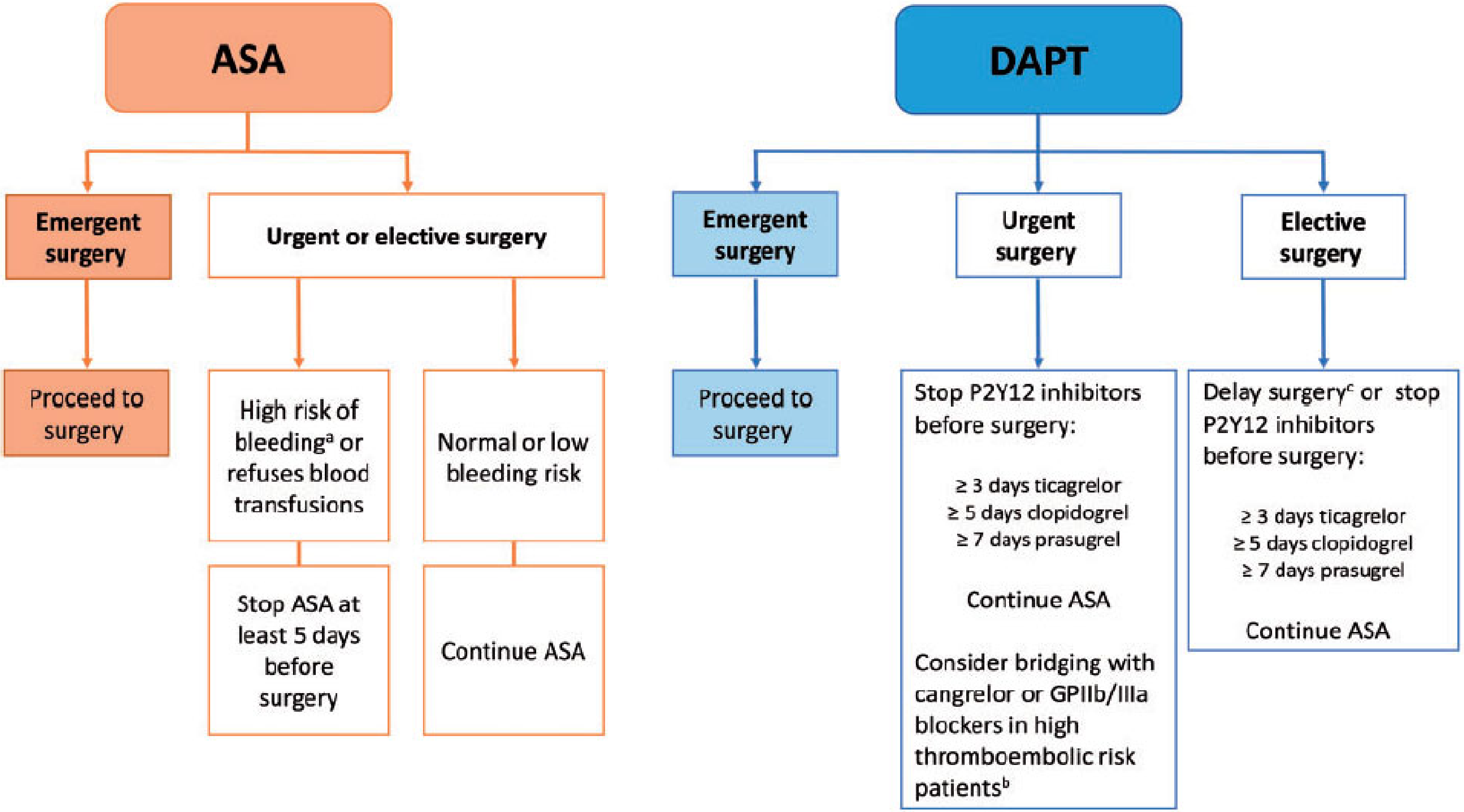
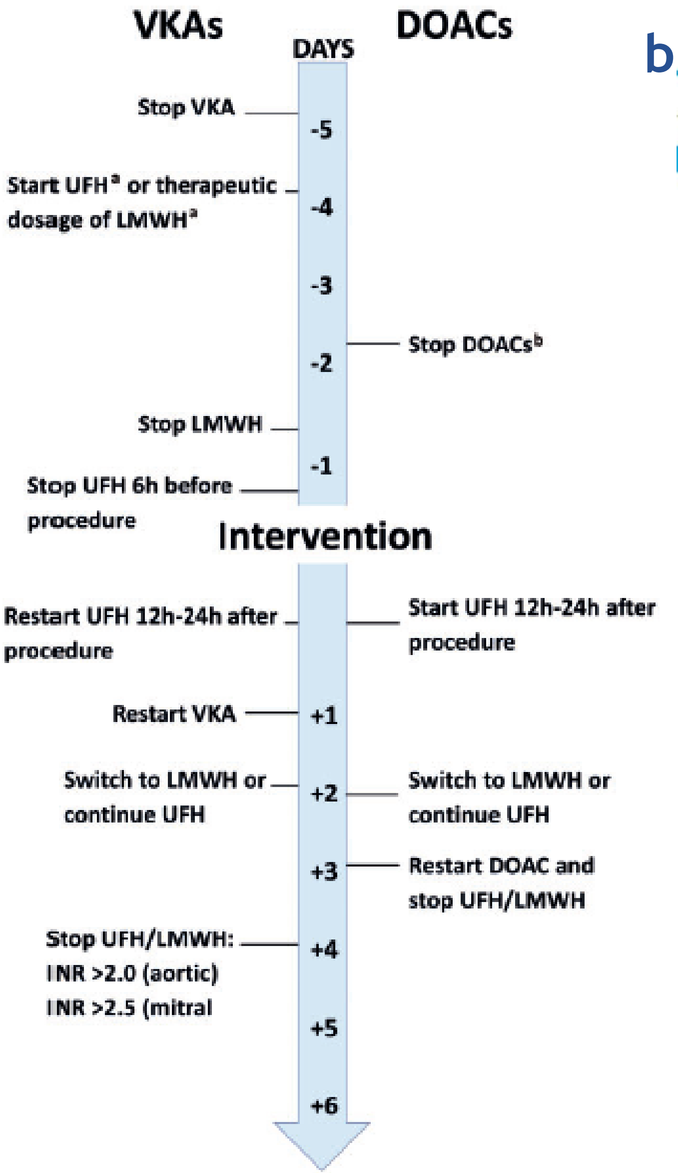


Figure 1: Management of antiplatelet therapy in patients having coronary artery bypass grafting surgery. [a]Complex and redo operations, severe renal insufficiency, haematological diseases and hereditary deficiencies in platelet function. [b]Recent stent implantation, recent thromboembolic event and alarming angiographic results. [c]Until the recommended DAPT period is completed. ASA: acetylsalicylic acid; DAPT: dual antiplatelet therapy; GPIIb/IIIa: glycoprotein IIb/IIIa.

Authors/Task Force Members. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery: The Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA). Eur J Cardiothorac Surg. 2017 Oct 3.

2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery



AVK (J-5) et AOD (J-2 à J-4)

Figure 2: Management of oral anticoagulation in patients with an indication for pre- and/or postoperative bridging (reproduced with permission from Sousa-Uva. Stuart J. Head, Milan Milojevic, Jean-Philippe Collet, Giovanni Landoni, Manuel Castella *et al.* 2017 EACTS Guidelines on Perioperative Medication in Adult Cardiac Surgery. *Eur J Cardiothorac Surg* 2017; doi:10.1093/ejcts/ezx314). [a]Bridging with UFH/LMWH should start when INR values are below specific therapeutic ranges. [b]Discontinuation should be prolonged to >72 h if creatinine clearance is 50–79 ml/min/1.73 m^2 or ≥96 h if creatinine clearance is <50 ml/min/1.73 m^2. DOACs: direct oral anticoagulants; INR: international normalized ratio; LMWH: low-molecular-weight heparin; UFH: unfractionated heparin; VKAs: vitamin K antagonists.

Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA), Boer C, Meesters MI, Milojevic M, Benedetto U, Bolliger D, et al. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. J Cardiothorac Vasc Anesth. 2018 Feb;32(1):88–120.

Original paper

Perfusion

Perfusion
1–7

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DOI: 10.1177/0267659114542457
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SAGE

Prevalence of preoperative anaemia in patients having first-time cardiac surgery and its impact on clinical outcome. A retrospective observational study

CJ Kim,[1] H Connell,[2] AD McGeorge[2] and R Hu[3]

28% patients anémiques

80% vs 38% transfusion

Abstract

The prevalence of anaemia is increasing globally. It has a close association with perioperative blood transfusion which, in turn, results in an increased risk of postoperative complications. Undesirable effects are not only limited to short-term, but also have long-term implications. Despite this, many patients undergo cardiac surgery with undiagnosed and untreated anaemia. We designed a retrospective, observational study to estimate the prevalence of anaemia in patients having cardiac surgery in Auckland District Health Board, blood transfusion rates and associated clinical outcome. Two hundred of seven hundred and twelve (28.1%) patients were anaemic. Red blood cell (RBC) transfusion rates were significantly higher in the anaemic group compared to the non-anaemic group (160 (80%) vs. 192 (38%), p-value <0.0001, RR (CI 95%) 2.133 (1.870-2.433)). Transfusion rates for fresh frozen plasma (FFP), cryoprecipitate and platelets were also higher in the anaemic group. Anaemia was significantly associated with the development of new infection (14 (7%) vs. 15 (2.9%), p-value 0.0193, RR (CI 95%) 2.389 (1.175-4.859)), prolonged ventilation time (47.01 hours vs. 23.59 hours, p-value 0.0076) and prolonged intensive care unit (ICU) stay (80.23 hours vs. 50.27, p-value 0.0011). Preoperative anaemia is highly prevalent and showed a clear link with significantly higher transfusion rates and postoperative morbidity. It is vital that a preoperative management plan for the correction of anaemia should be sought to improve patient safety and outcome.

JAMA®

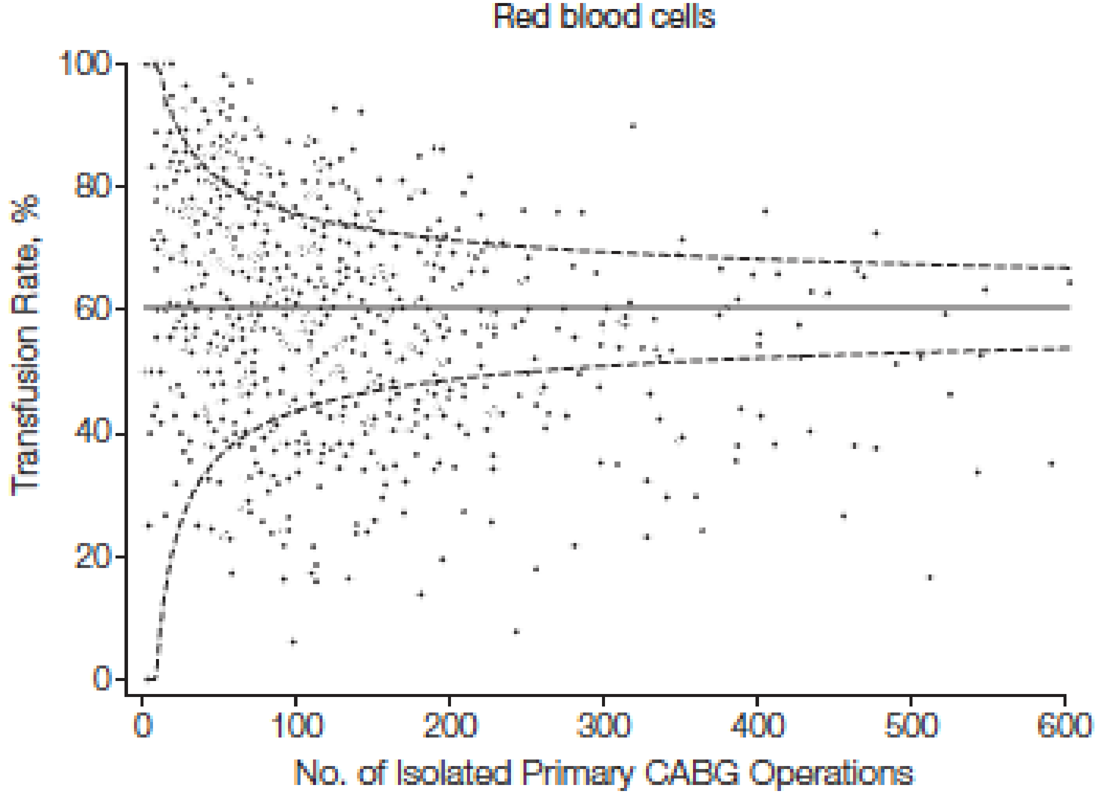
Online article and related content
current as of October 19, 2010.

Variation in Use of Blood Transfusion in Coronary Artery Bypass Graft Surgery

Elliott Bennett-Guerrero; Yue Zhao; Sean M. O'Brien; et al.

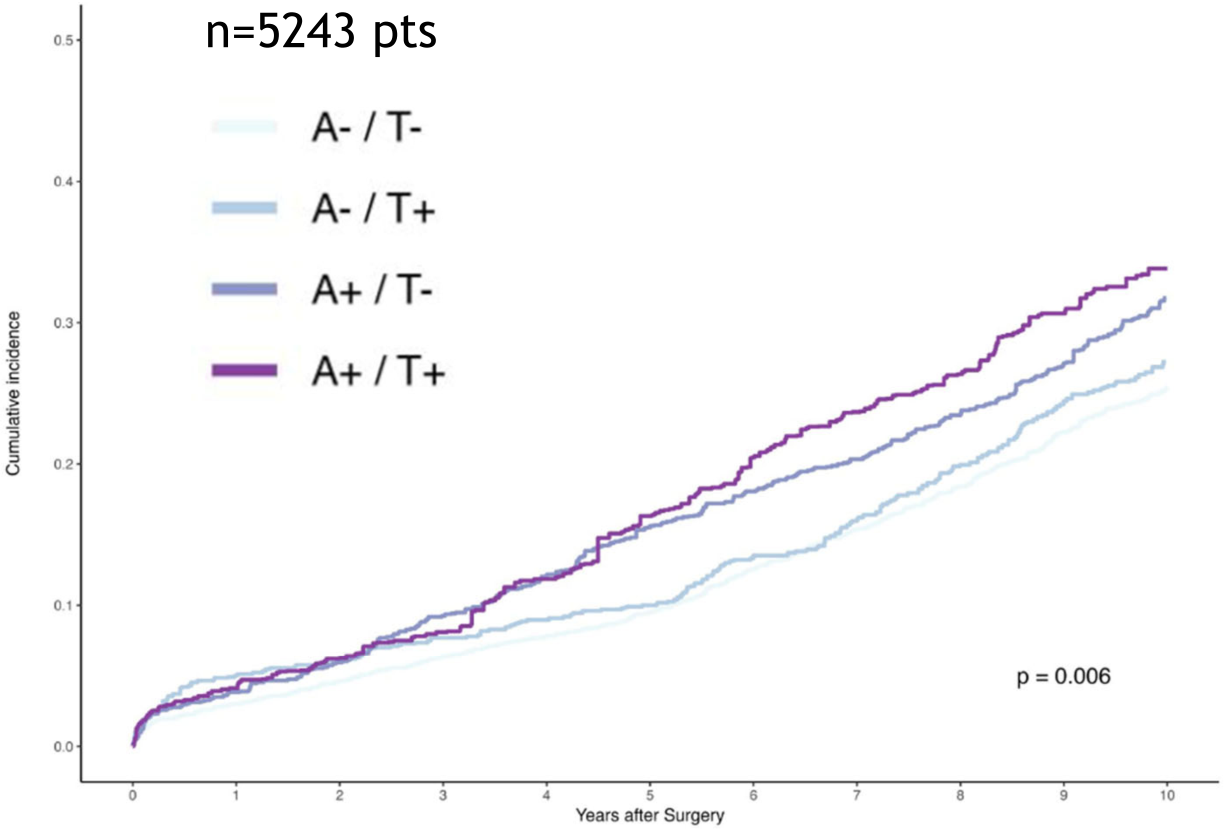
JAMA. 2010;304(14):1568-1575 (doi:10.1001/jama.2010.1406)

Figure 1. Observed Variation in Hospital-Specific Transfusion Rates for Primary Isolated CABG Surgery With Cardiopulmonary Bypass During 2008 (N=798 Sites)



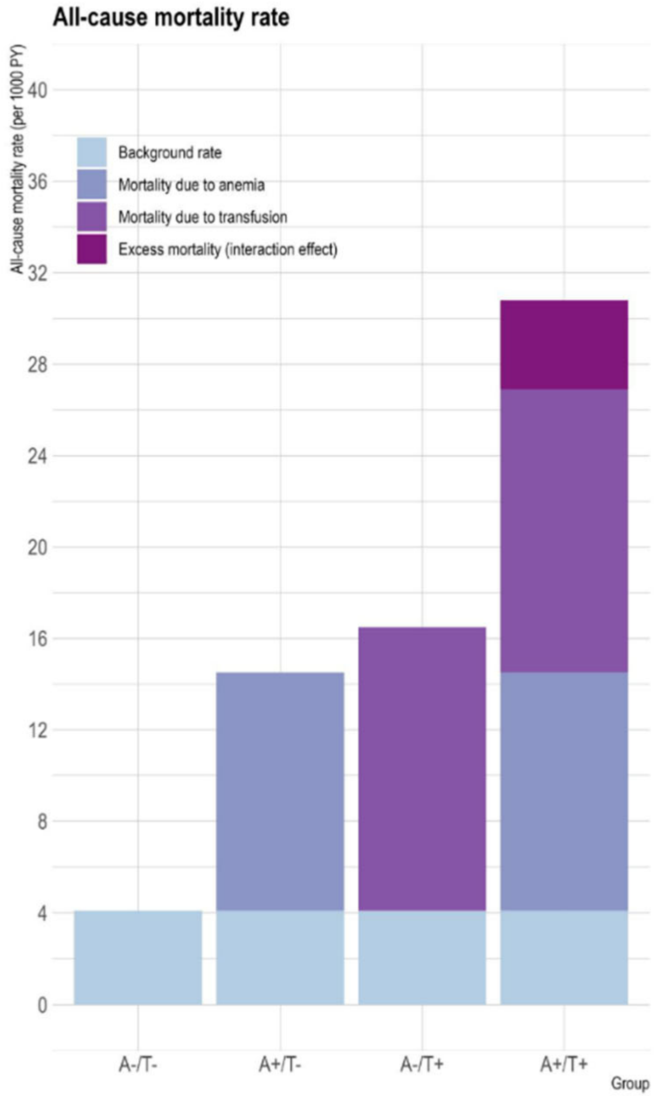
The additive effects of anaemia and transfusion on long-term survival after coronary artery bypass surgery

Abreu A et al *European Journal of Cardio-Thoracic Surgery 2024, 65(3)*



Numbers at risk	0	1	2	3	4	5	6	7	8	9	10
A- / T-	2773	2717	2678	2633	2593	2549	2438	2287	2033	1781	1555
A- / T+	836	798	788	775	764	754	721	685	579	467	392
A+ / T-	1063	1014	991	951	919	880	844	800	720	647	558
A+ / T+	583	532	511	494	473	448	411	369	300	236	188

Figure 4: Long-term survival in inverse probability weighted cohort.



Définition universelle du saignement péri-opératoire

Perioperative Management Kinnunen et al

Clinical significance and determinants of the universal definition of perioperative bleeding classification in patients undergoing coronary artery bypass surgery

Eeva-Maija Kinnunen, MS,[a] Tatu Juvonen, MD, PhD,[a] Kari Eino Juhani Airaksinen, MD, PhD,[b] Jouni Heikkinen, MD, PhD,[a] Ulla Kettunen, RN,[a] Giovanni Mariscalco, MD, PhD,[c] and Fausto Biancari, MD, PhD[a]

Independent predictors of high UDPB classes

- Increased age
- Low hemoglobin
- **On-pump surgery *(full anticoagulation protocol)***
- Potent antiplatelet drug pause of <5 days
- Warfarin pause <2 days

Conclusions: High UDPB classes were associated with significantly poorer immediate and late outcomes. The UDPB classification seems to be a valuable research tool to estimate the severity of bleeding and its prognostic impact affect after coronary surgery. (J Thorac Cardiovasc Surg 2014;148:1640-6)

Kinnunen E-M, et al. Clinical significance and determinants of the universal definition of perioperative bleeding classification in patients undergoing coronary artery bypass surgery. J Thorac Cardiovasc Surg 2014;148(4):1640–2.

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Que peut-on faire ?

Comment gérer de façon optimale l'anticoagulation en CEC au 21ème siècle?

Les guidelines !

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful and effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence/general agreement that the given treatment/procedure is not useful/effective and may sometimes be harmful.	Is not recommended

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	The consensus of expert opinion and/or small studies, retrospective studies, registries.

Recommendations	Class[a]	Level[b]	Ref[c]
Implementation of institutional measures to reduce haemodilution by fluid infusion and CPB during cardiac surgery to reduce the risk of bleeding and the need for transfusions is recommended.	I	C	
The use of a closed extracorporeal circuit may be considered to reduce bleeding and transfusions.	IIb	B	[112, 113]
The use of a biocompatible coating to reduce perioperative bleeding and transfusions may be considered.	IIb	B	[114–116]
The routine use of cell salvage should be considered to prevent transfusions.	IIa	B	[117–119]
(Modified) ultrafiltration may be considered as part of a blood conservation strategy to minimize haemodilution.	IIb	B	[120–122]
Retrograde and antegrade autologous priming should be considered as part of a blood conservation strategy to reduce transfusions.	IIa	A	[123–125]
Normothermia during CPB (temperature >36° C) and maintenance of a normal pH (7.35–7.45) may contribute to a reduced risk of postoperative bleeding.	IIb	B	[126, 127]

- Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA), Boer C, Meesters MI, Milojevic M, Benedetto U, Bolliger D, et al. 2017
- EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. J Cardiothorac Vasc Anesth. 2018 Feb;32(1):88–120.

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Interactive CardioVascular and Thoracic Surgery 19 (2014) 788–794
doi:10.1093/icvts/ivu266 Advance Access publication 14 August 2014

ORIGINAL ARTICLE – ADULT CARDIAC

A structured blood conservation programme reduces transfusions and costs in cardiac surgery

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[b] Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
[c] Department of Cardiothoracic Anaesthesia and Intensive Care, Sahlgrenska University Hospital, Gothenburg, Sweden

The programme included:

- Education risk/benefit
- Guidelines respect
- Transfusion log
  - → Indication
  - → Patient status
  - → Prescribing physician

But heparin 350 IU/Kg and protamine 1:1

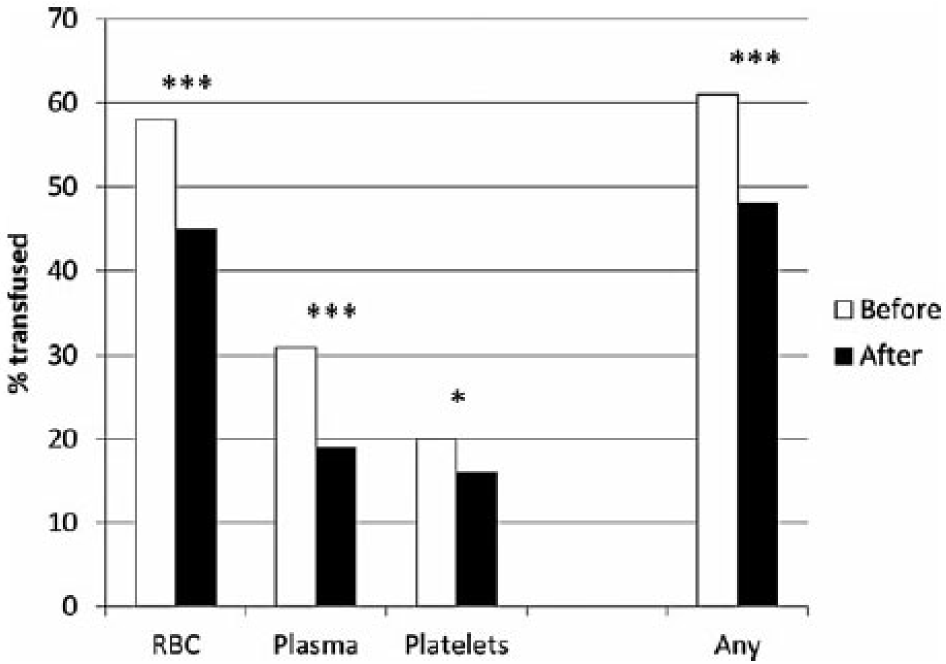
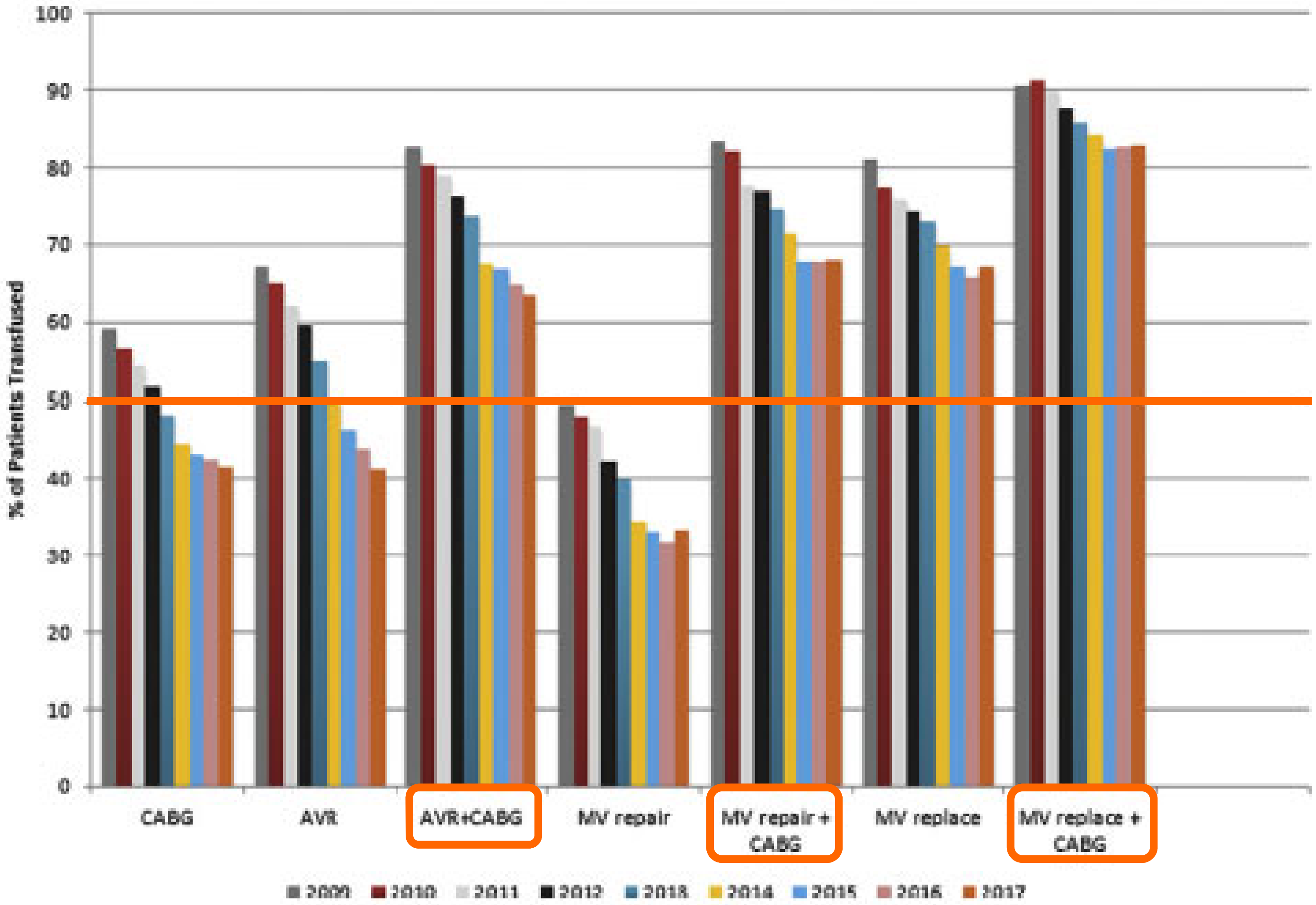


Figure 2: Percentage of patients transfused with red blood cells (RBCs), plasma, platelets and any blood product before (white bars) and after (black bars) the blood conservation programme was started. *P <0.05, ***P <0.001.

Où en sommes-nous dans la vie réelle ?



D'Agostino RS et al. The Society of Thoracic Surgeons Adult Cardiac Surgery Database: 2019 Update on Outcomes and Quality. Ann Thorac Surg. 2019;107(1):24-32.

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Deux stratégies différentes

1. Réduction de la dose d'héparine
2. Réduction ciblée de l'anticoagulation

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1. Réduction de la dose d'héparine

- Habituellement la moitié de la dose habituelle d'héparine
- 150 UI/Kg au lieu de 300 UI/Kg
- Gestion de la CEC inchangée par ailleurs, excepté l'utilisation systématique de circuits pré-héparinés

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Sans changer le seuil d'anticoagulation
Possibilité de réduire la dose d'héparine

Excess of heparin dose to reach ACT>480s

A starting dose of 200 IU/kg of heparin and if necessary one 50 IU/kg increment achieved target ACT in 81.5% of patients.

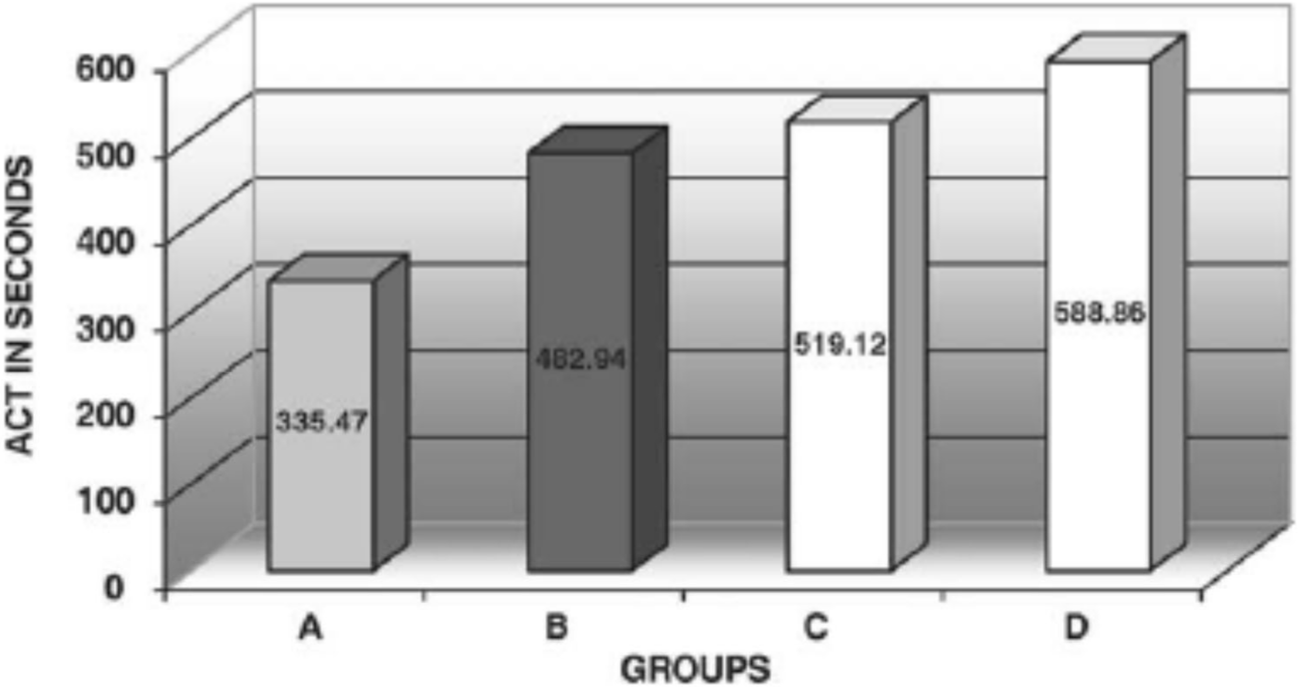

Fig. 2. Mean ACT after the initial dose of heparin in different groups.

Shuhaibar MN, et al. How much heparin do we really need to go on pump? A rethink of current practices. Eur J Cardiothorac Surg. 2004;26(5):947–50.

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Plus grande expérience en réduction d'héparine combinée à l'utilisation de CEC préhéparinée

Heparinized cardiopulmonary bypass circuits and low systemic anticoagulation: An analysis of nearly 6000 patients undergoing coronary artery bypass grafting

Eivind Øvrum, MD, PhD, Geir Tangen, MD, Stein Tølløfsrud, MD, PhD, Bjørn Skeie, MD, PhD, Mari Anne L. Ringdal, CCP, Reidar Istad, CCP, and Rolf Øystese, CCP

Objective: Heparin coating of cardiopulmonary bypass circuits reduces the inflammatory response and increases the thromboresistance during extracorporeal circulation. These properties enables a lower systemic heparin dose, which has been shown to reduce the need for blood transfusions. Experience with this technique accumulated over 11 years has been analyzed.

Methods: All patients underwent on-pump coronary artery bypass grafting with heparin-coated circuits. Apart from some patients receiving a high intraoperative dose of aprotinin, the systemic heparin dose was reduced, with a lower level of an activated clotting time of 250 seconds during extracorporeal circulation. The overall strategy aimed at a fast-track regimen, with early extubation, minimal use of blood transfusions, and rapid postoperative recovery.

Results: Altogether, 5954 patients were included; 1131 (19.0%) were female (median age, 70 years), and 4823 were male (median age, 65 years). The median additive EuroSCORE was 3 (range, 0–14; mean 3.5 ± 2.5). No significant signs of clotting were seen in any part of the extracorporeal circuit. Bank blood products were given to 427 (7.2%) patients. Median extubation time was 1.7 hours. The stroke rate was 1.0%, transient neurologic deficits occurred in 0.7%, and perioperative myocardial infarction occurred in 1.2%. On the fifth day, 88.1% of the patients were physically rehabilitated and ready for discharge. Thirty-day mortality was 0.9% (54 patients).

Conclusions: The experience with this patient cohort including mostly low- to medium-risk patients with a relatively short cardiopulmonary bypass time indicates that coronary artery bypass grafting performed with heparin-coated circuits and reduced level of systemic heparinization is safe and results in a very satisfactory clinical course. No signs of clotting or other technical incidents were recorded. (J Thorac Cardiovasc Surg 2010;■:1-5)

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2. Réduction ciblée du niveau d'anticoagulation

- Détermination d'un ACT cible réduit
- *Reduced Goal Directed Anticoagulation*
- Pratique non fondée sur le poids du patient pour administrer une dose initiale d'héparine
- Pratique d'anticoagulation adaptée à chaque patient selon les circonstances

  Recours à un monitorage dédié

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Les 10 commandements

1. ACT cible @ 250s pour les cœurs fermés. ACT cible @ 350s pour cœurs ouverts et redux
2. Utilisation d'un monitorage dédié permettant une titration précise de l'héparine et de la protamine (ratio protamine:heparine @ 0.3/0.6:1)
3. Utilisation d'un antifibrinolytique (ac. tranexamique)
4. CEC en normothermie
5. Contrôle des aspiration chirurgicales péricardiques et utilisation d'un Cell-Saver

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Les 10 commandements

6. CEC préhéparinée avec oxygénateur à membrane réduisant l'interface air-sang (circuit clos, décharge VG par déclivité dans réservoir souple: pas de retour veineux actif)
7. Limiter l'hémodilution autant que possible (attention au remplissage préopératoire, rétropriming)
8. Les purges cavitaires au CO_2 sont hautement thrombogéniques et doivent être évitées
9. Eviter la stagnation de sang dans le circuit, rincer et recirculer après arrêt de la CEC
10. Respecter une hémostase chirurgicale rigoureuse !

1. ACT cible @ 250 s
Cœurs fermés (pontages)

Effect of Anticoagulation Protocol on Outcome in Patients Undergoing CABG With Heparin-Bonded Cardiopulmonary Bypass Circuits

Gabriel S. Aldea, MD, Paul O'Gara, CCP, Oz M. Shapira, MD, Patrick Treanor, CCP, Ashraf Osman, MD, Eva Patalis, MD, Charles Arkin, MD, Rhea Diamond, PhD, Viken Babikian, MD, Harold L. Lazar, MD, and Richard J. Shemin, MD

Departments of Cardiothoracic Surgery, Pathology, and Neurology, Boston University Medical Center, Boston, Massachusetts

Essai clinique randomisé prospectif : ACT @ 250s *vs* ACT @ 450s

- Moins de transfusion: **24.2%** *vs* 35.8% (p<0.05)
- Moins d'évènements emboliques**: 0.81%** *vs* 5.0% (p<0.05)
- Pas de corrélation entre production de thrombine et anticoagulation
- Pas de différence sur embolisation cérébrale et fonction cognitive

58 patients (full anticoagulation profile = 28, lower anticoagulation profile = 30) by measuring thrombin-antithrombin complexes and prothrombin fragment 1.2. Levels of these markers also were correlated with the activated clotting time during cardiopulmonary bypass.

Results. Preoperative and intraoperative risk profiles and other characteristics were similar in both groups, with more than 60% of patients undergoing nonelective operation. Compared with the full anticoagulation protocol group, patients in the lower anticoagulation proto-

when used appropriately, patients who are treated with HBCs and a lower anticoagulation protocol have a lower incidence and magnitude of homologous transfusion and are not at any added risk for clinical, hematologic (thrombin-antithrombin complex and fragment 1.2 measurements), or microscopic (transcranial Doppler analyses) thromboembolic complications or for neurologic or neuropsychologic deficits.

(Ann Thorac Surg 1998;65:425–33)

Aldea GS, et al. Effect of anticoagulation protocol on outcome in patients undergoing CABG with heparin-bonded cardiopulmonary bypass circuits. Ann Thorac Surg. 1998;65(2):425-33.

1. ACT cible @ 350 s
Cœurs ouverts et redux

- Valeur empirique !
- Prend en compte l'impact de l'interface air-sang sur l'activation de la coagulation
- Dérive en partie de l'étude de Schönberger

Un circuit clos/circuit ouvert:

1. **Réduit l'activation de**
   - **complément**
   - **neutrophiles**
   - **plaquettes**
   - **fibrinolyse**
2. **Diminue l'hémolyse et le saignement post-op.**
3. **Améliore la clearance de l'endotoxine**

Schönberger JP, Everts PA, Hoffmann JJ. Systemic blood activation with open and closed venous reservoirs. Ann Thorac Surg. 1995 Jun 1;59(6):1549-55.

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2. Monitorage adapté pour l'héparine et la protamine
Diminuer le ratio protamine/héparine

- Identifier la réponse individuelle à l'héparine pour atteindre un ACT cible
- Calcul de la dose initiale en mettant le sang du patient au contact de deux doses d'héparine afin d'établir une courbe dose –réponse
- En fin de procédure, détermination de l'héparine résiduelle en vue de sa neutralisation par la dose adéquate de protamine

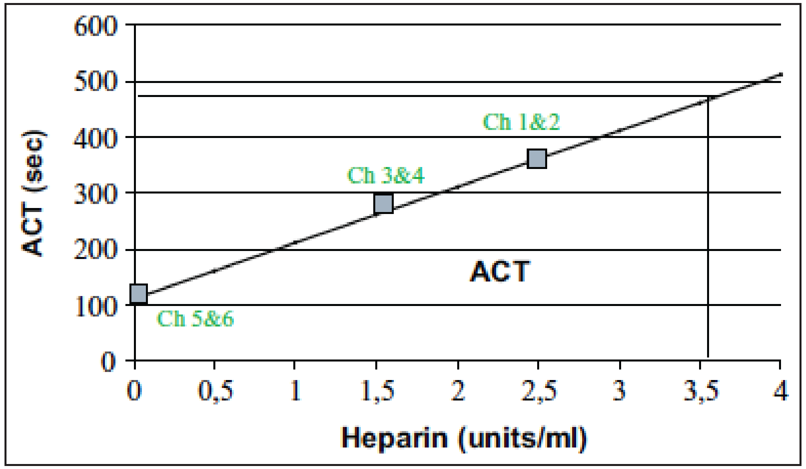

Figure 1. Heparin dose response (HDR) curve

Noui N et al. Anticoagulation monitoring during extracorporeal circulation with the Hepcon/HMS device. Perfusion 2012;27(3):214-20.

2. Monitorage adapté pour l'héparine et la protamine
Diminuer le ratio protamine/héparine

44 pts: PAC ou RVA ACT@400s	HMS (n=22)	Hémocron (n=22)
Durée fermeture (min)	42 ± 15	68 ± 27 *
Durée clampage (min)	56 ± 30	62 ± 28
Ratio protamine/héparine	0,62 ± 0,13	1 ± 0.11 *
Saignement (mL)	804 ± 729	1416 ± 1103 *
Transfusion (U/Pt)	1,04 ± 1,5	2,1 ± 1,87 *

*HMS: Heparin Management System ; *:p<0,05*

Noui N et al. Anticoagulation monitoring during extracorporeal circulation with the Hepcon/HMS device. Perfusion 2012;27(3):214-20.

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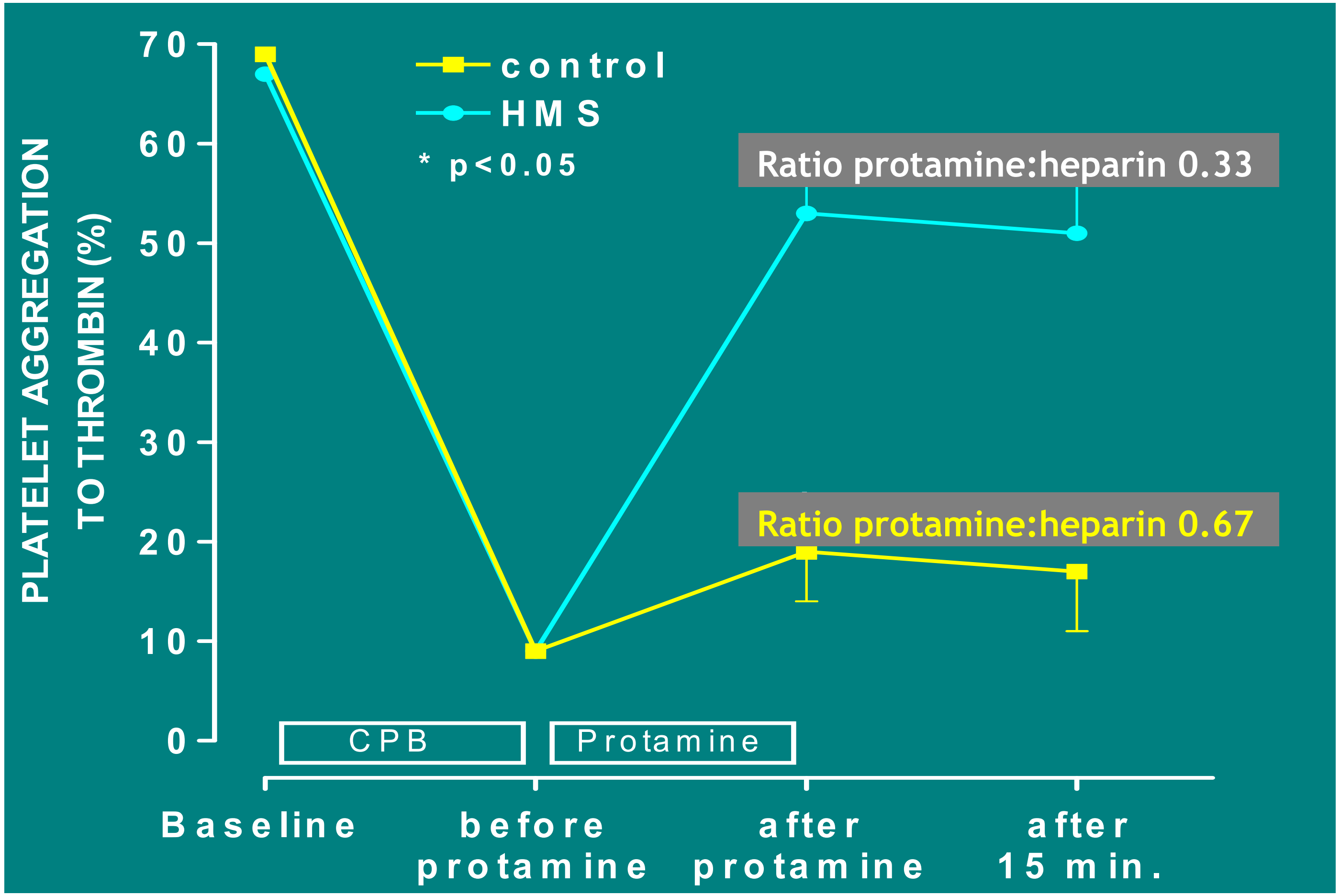
2. Monitorage adapté pour l'héparine et la protamine

Effet de la protamine en excès sur les plaquettes



Shigeta O, et al. Low-dose protamine based on heparin-protamine titration method reduces platelet dysfunction after cardiopulmonary bypass. J Thorac Cardiovasc Surg. 1999;118(2):354-60.

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3. Anti-fibrinolytique

- Acide tranexamique: antifibrinolytique synthétique bon marché, qui inhibe le t-PA et l'activité de la plasmine, entrainant une réduction du saignement postopératoire
- Aprotinine: inhibiteur non spécifique de protéases, issue du poumon bovin, qui interagit avec les sites actifs de la plasmine, et de la kallikréine. Couteux, surtout en protocole dit de Royston (>8 MU), anti-inflammatoire à doses élevées seulement.
- Aprotinine retirée du marché à la fin des années 2000, puis réintroduit récemment
- Augmentation de la mortalité avec l'aprotinine *vs* acide tranexamique alors que peu d'effet supplémentaire sur la réduction du saignement
- Les équipes ont appris à s'en passer dans la grande majorité des cas !

Fergusson DA et al. N Engl J Med. 2008;358(22):2319-31.
Takagi H et al. Interact Cardiovasc Thorac Surg. 2009;9(1):98-101. Benedetto U et al. J Am Heart Assoc. 2018;7(5):e007570.

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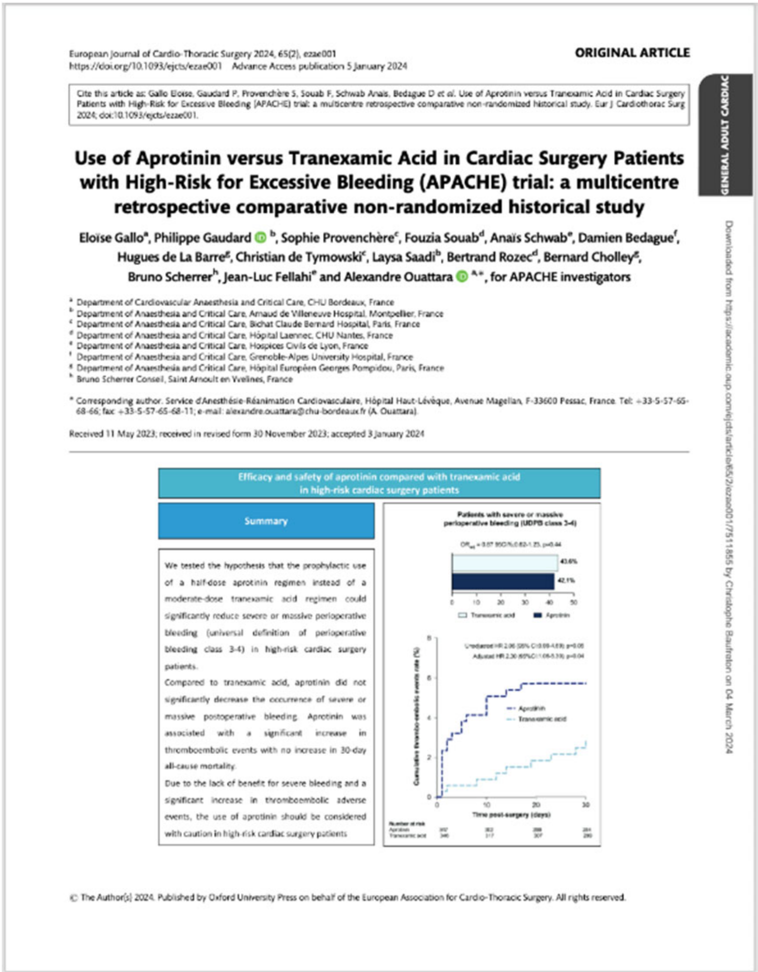
3. Anti-fibrinolytique
Aprotinine vs Ac Tranexamique (APACHE)


European Journal of Cardio-Thoracic Surgery 2024, 65(2), ezae001
https://doi.org/10.1093/ejcts/ezae001 Advance Access publication 5 January 2024

ORIGINAL ARTICLE

GENERAL ADULT CARDIAC

Cite this article as: Gallo Eloïse, Gaudard P, Provenchère S, Souab F, Schwab Anaïs, Bedague D *et al.* Use of Aprotinin versus Tranexamic Acid in Cardiac Surgery Patients with High-Risk for Excessive Bleeding (APACHE) trial: a multicentre retrospective comparative non-randomized historical study. Eur J Cardiothorac Surg 2024; doi:10.1093/ejcts/ezae001.

Use of Aprotinin versus Tranexamic Acid in Cardiac Surgery Patients with High-Risk for Excessive Bleeding (APACHE) trial: a multicentre retrospective comparative non-randomized historical study

Eloïse Gallo[a], Philippe Gaudard[b], Sophie Provenchère[c], Fouzia Souab[d], Anaïs Schwab[e], Damien Bedague[f], Hugues de La Barre[g], Christian de Tymowski[c], Laysa Saadi[b], Bertrand Rozec[d], Bernard Cholley[g], Bruno Scherrer[h], Jean-Luc Fellahi[e] and Alexandre Ouattara[a,*], for APACHE investigators

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Received 11 May 2023; received in revised form 30 November 2023; accepted 3 January 2024

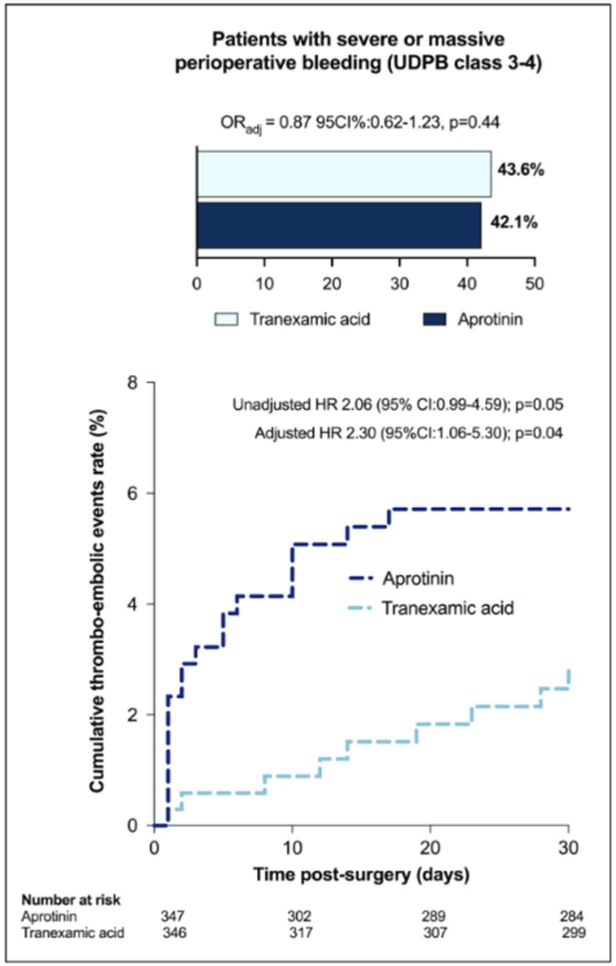
Efficacy and safety of aprotinin compared with tranexamic acid in high-risk cardiac surgery patients

Summary

We tested the hypothesis that the prophylactic use of a half-dose aprotinin regimen instead of a moderate-dose tranexamic acid regimen could significantly reduce severe or massive perioperative bleeding (universal definition of perioperative bleeding class 3-4) in high-risk cardiac surgery patients.

Compared to tranexamic acid, aprotinin did not significantly decrease the occurrence of severe or massive postoperative bleeding. Aprotinin was associated with a significant increase in thromboembolic events with no increase in 30-day all-cause mortality.

Due to the lack of benefit for severe bleeding and a significant increase in thromboembolic adverse events, the use of aprotinin should be considered with caution in high-risk cardiac surgery patients



Gallo, E. *et al*. Use of Aprotinin Versus Tranexamic Acid in Cardiac Surgery Patients with High-Risk for Excessive Bleeding (APACHE trial): A multicentre retrospective comparative non-randomised historical study. *Eur. J. Cardio-Thorac. Surg.* ezae001 (2024).

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4. Normothermie

SYSTEMATIC REVIEW

Cardiovascular Therapeutics

Benefits and Risks of Maintaining Normothermia during Cardiopulmonary Bypass in Adult Cardiac Surgery: A Systematic Review

Kwok M. Ho[1] & Jen Aik Tan[2]

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2 Intensive Care Unit Medical Officer, Department of Intensive Care Medicine, Royal Perth Hospital, Perth, WA 6000, Australia

Keywords
Stroke; cardiopulmonary bypass; hemorrhage; transfusion.

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doi: 10.1111/j.1755-5922.2009.00114.x

Cardiopulmonary bypass is associated with significant morbidities, and the ideal temperature management during cardiopulmonary bypass remains uncertain. This review assessed the benefits and risks of maintaining normothermia during cardiopulmonary bypass in adult cardiac surgery. A total of 6731 patients from 44 randomized controlled trials in 14 countries, comparing normothermic (>34°C) and hypothermic (≤34°C) cardiopulmonary bypass in cardiac surgery (>18 years of age), were identified from MEDLINE (1966 to August 10, 2009), EMBASE (1988 to August 10, 2009), and Cochrane controlled trials register and subject to meta-analysis. Two investigators examined all studies and extracted the data independently. Mortality after normothermic and hypothermic bypass was not significantly different (1.4% vs. 1.9% respectively, relative risk [RR] 1.38, 95% confidence interval [CI] 0.94–2.04, $I^2 = 0\%$, $P = 0.10$). Hypothermic bypass was, however, associated with an increased risk of allogeneic red blood cells (RR 1.19, 95% CI 1.07–1.34, $I^2 = 0\%$, $P = 0.002$), fresh frozen plasma (RR 1.54, 95% CI 1.06–2.24, $I^2 = 7.7\%$, $P = 0.02$), and platelet transfusion (RR 2.53, 95% CI 1.26–5.06, $I^2 = 44\%$, $P = 0.009$). The risk of stroke, cognitive decline, atrial fibrillation, use of inotropic support or intra-aortic balloon pump, myocardial infarction, all-cause infections, and acute kidney injury after cardiac surgery was not significantly different between the two groups. The differences in the bypass time and targeted perfusion temperature were not significantly related to the risk of mortality and stroke. The current evidence suggests that maintaining normothermia during cardiopulmonary bypass in adult cardiac surgery is as safe as that of hypothermic surgery, and associated with a reduced risk of allogeneic blood transfusion.

Review method

Randomized controlled trials comparing normothermic (>34°C) and hypothermic (≤34°C) cardiopulmonary bypass in cardiac surgery (>18 years of age) from MEDLINE (1966 to August 10, 2009), EMBASE (1988 to August 10, 2009), and Cochrane controlled trials register were included without any language restrictions. Two researchers searched the literature and extracted the data independently.

Take home message

The current evidence suggests that maintaining hypothermia during cardiopulmonary bypass in adult cardiac surgery is associated with an increased risk of

TAKE HOME MESSAGE

The current evidence suggests that maintaining hypothermia during cardiopulmonary bypass in adult cardiac surgery is associated with an increased risk of bleeding and allogeneic blood transfusion but without significant benefits in reducing the risk of stroke, cognitive decline, atrial fibrillation, use of inotropic support or intra-aortic balloon pump, myocardial infarction, all- cause infections, and acute kidney injury after cardiac surgery.

Normothermia during CPB (temperature >36° C) and maintenance of a normal pH (7.35–7.45) may contribute to a reduced risk of postoperative bleeding.	IIb	B

Ho KM, Tan JA. Benefits and Risks of Maintaining Normothermia during Cardiopulmonary Bypass in Adult Cardiac Surgery: A Systematic Review. Cardiovasc Ther. 2009;29(4):260–79.

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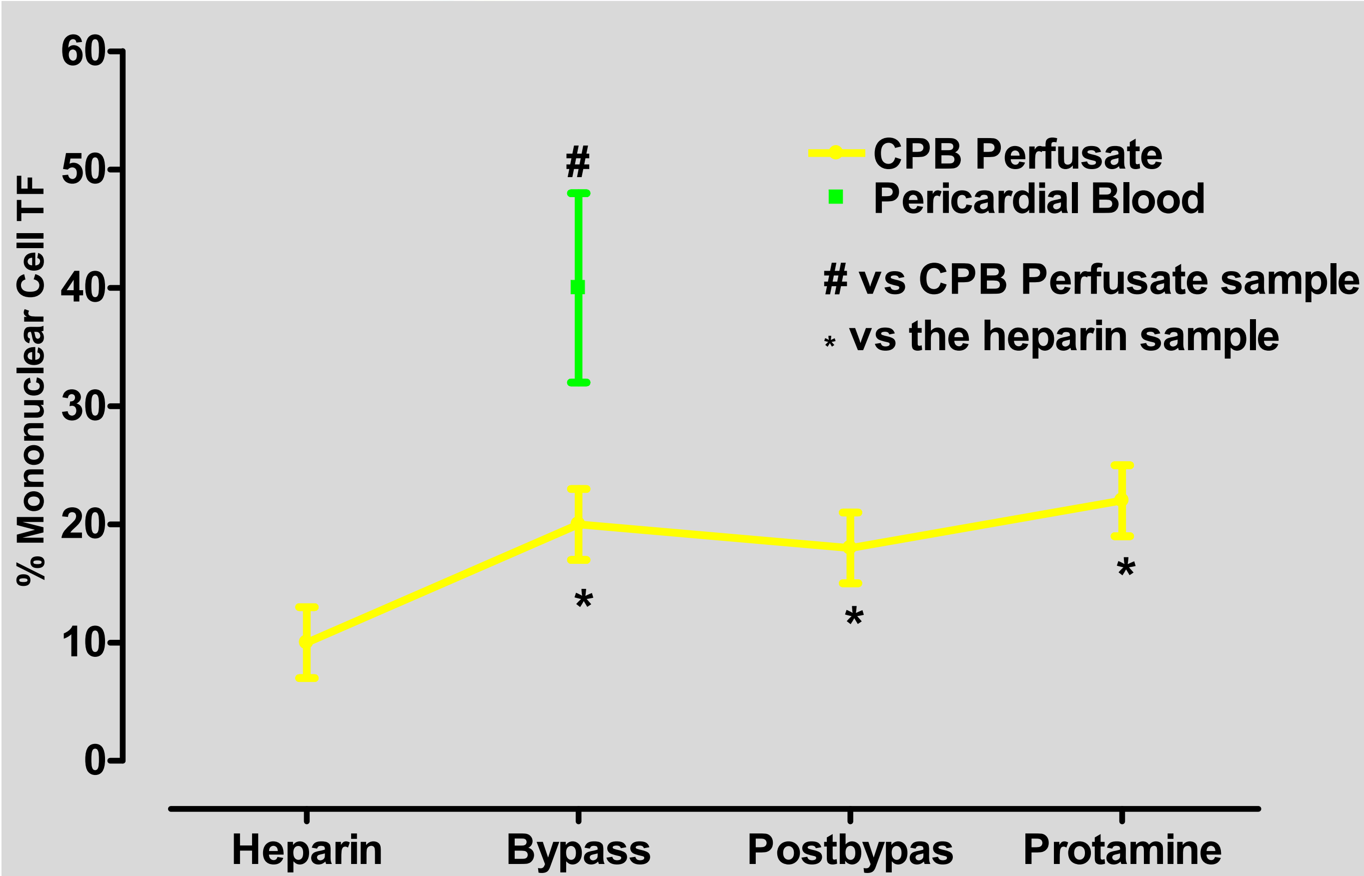
5. Gestion des aspirations

Cavité péricardique et voie tissulaire de la coagulation



Facteur tissulaire exprimé par les monocytes

Chung JH, Gikakis N, Rao AK, Drake TA, Colman RW, Edmunds LH. Pericardial blood activates the extrinsic coagulation pathway during clinical cardiopulmonary bypass. Circulation 1996;93(11):2014–8.

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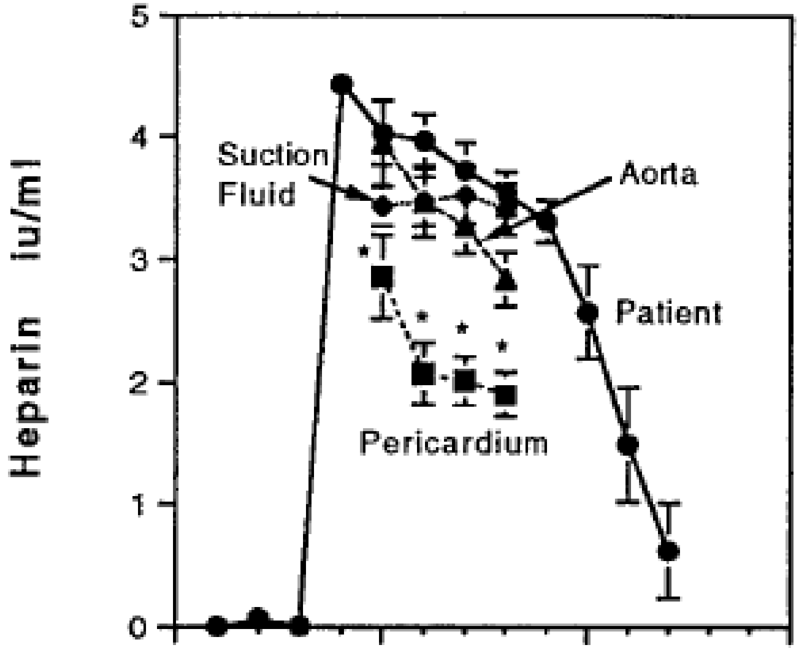
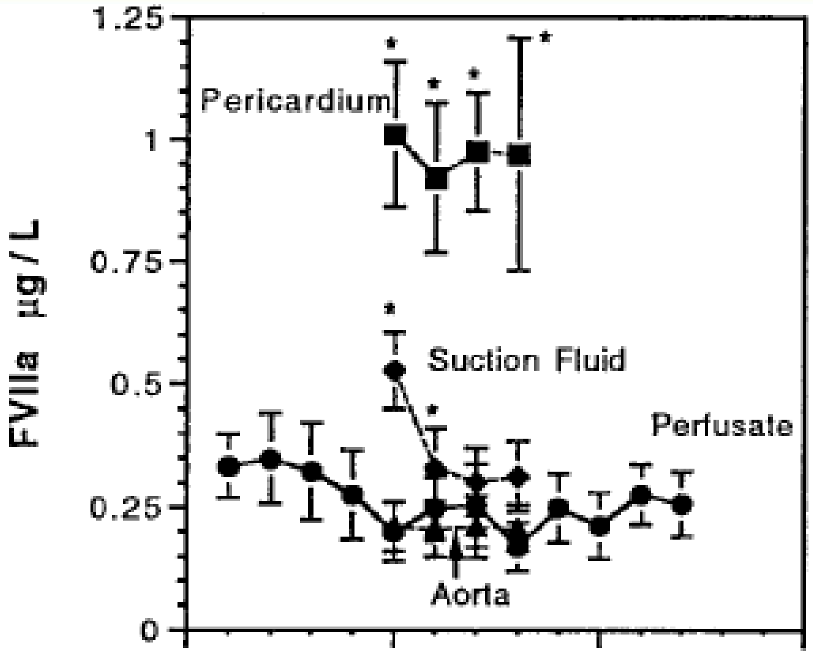
5. Gestion des aspirations

Héparine et activation voie tissulaire dans le péricarde



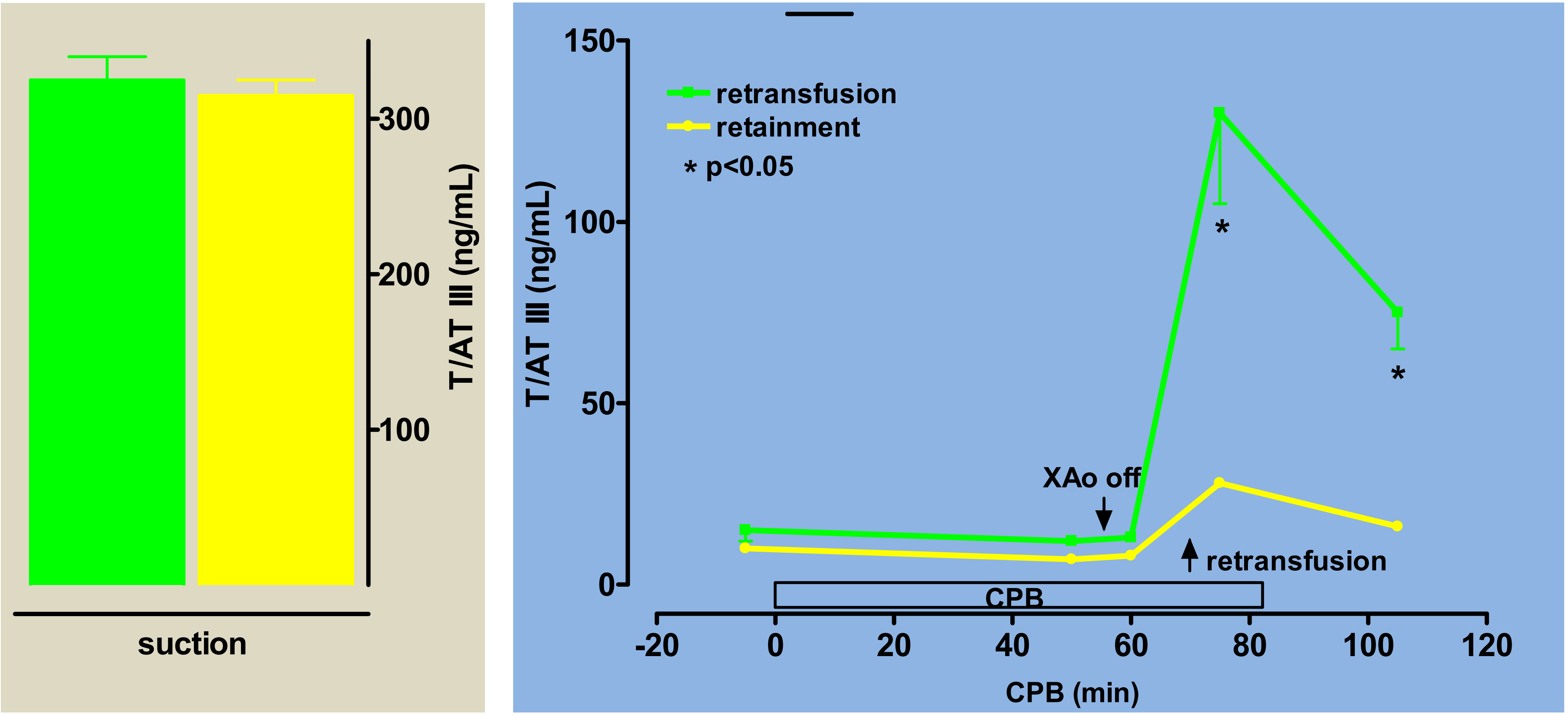


1. **Voie veineuse centrale**
2. **Aorte (outflow coronaire de CPG rétrograde)**
3. **Péricarde**
4. **Aspirations CEC**

Philippou H, et al. Two-chain factor VIIa generated in the pericardium during surgery with cardiopulmonary bypass : relationship to increased thrombin generation and heparin concentration. Arterioscler Thromb Vasc Biol. 1999 Feb 1;19(2):248-54.

5. Gestion des aspirations

Impact de la gestion des aspirations du sang péricardiques sur l'activation de la coagulation dans le sang circulant



de Haan J et al. Retransfusion of suctioned blood during cardiopulmonary bypass impairs hemostasis. Ann Thorac Surg. 1995 Apr;59(4):901–7.

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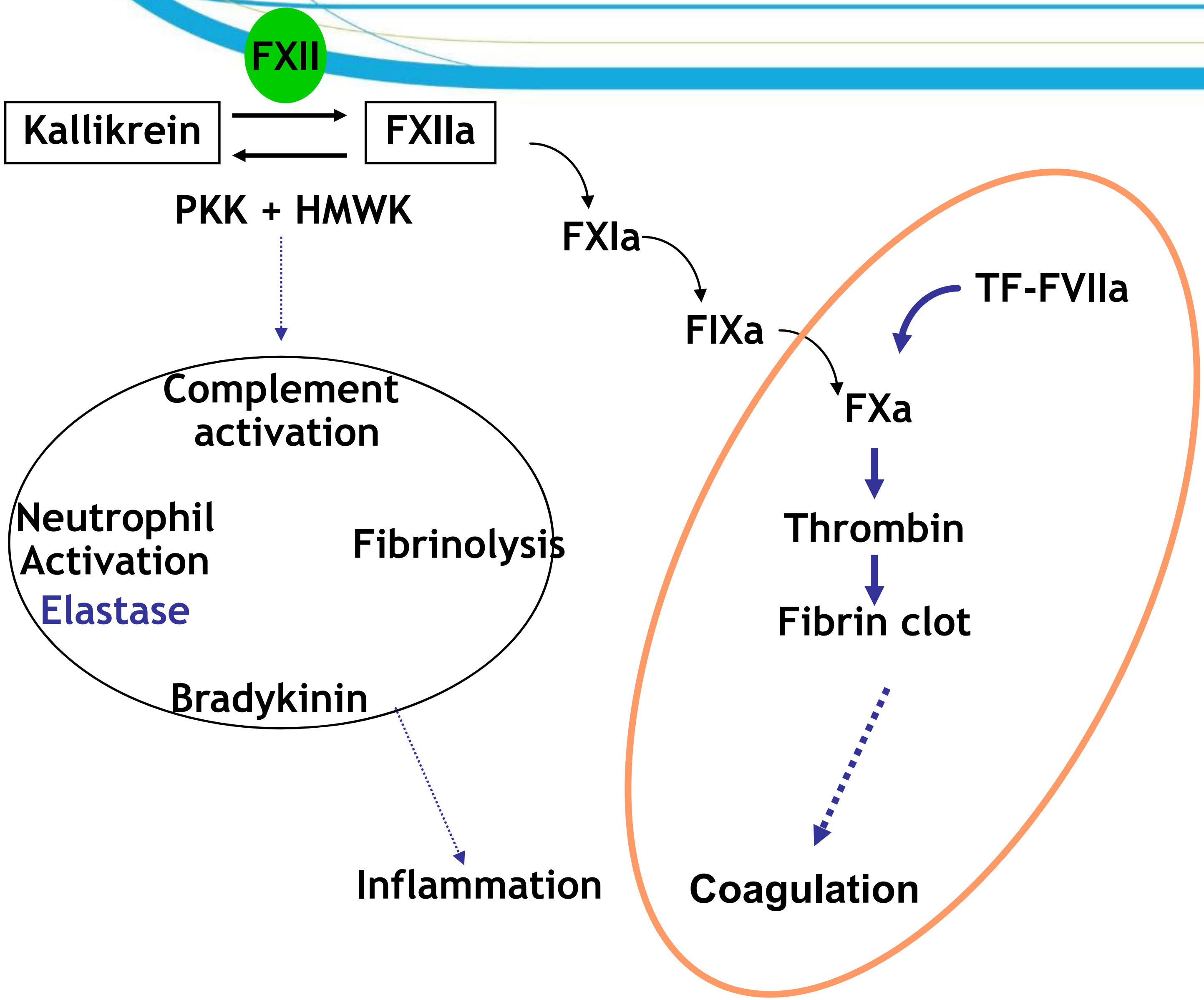
Activation de la coagulation en CEC

Place de la voie extrinsèque / intrinsèque



5. Gestion des aspirations et embolies

Comparaison cell-saver et filtres artériels

Dogs

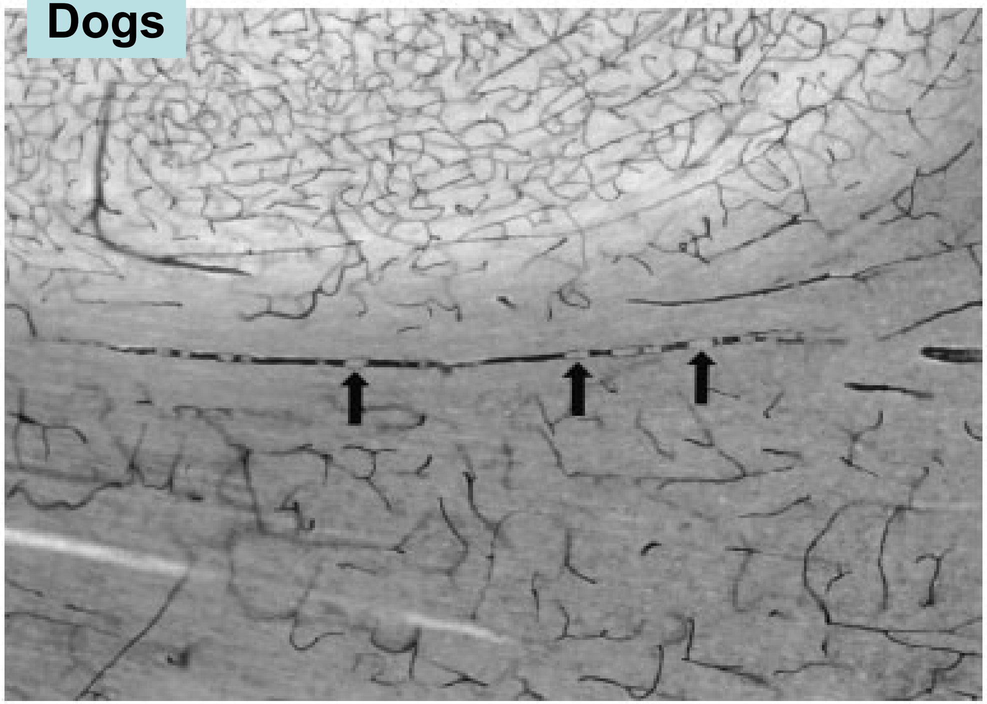


Fig 1. Representative photomicrograph of canine brain tissue with SCADs, indicating by arrows, after CPB and return of scavenged blood (alkaline phosphatase-stained, 100 μm thick).

SCAD: Small capillary and arteriolar dilations

Arterial filters | Cell-saver

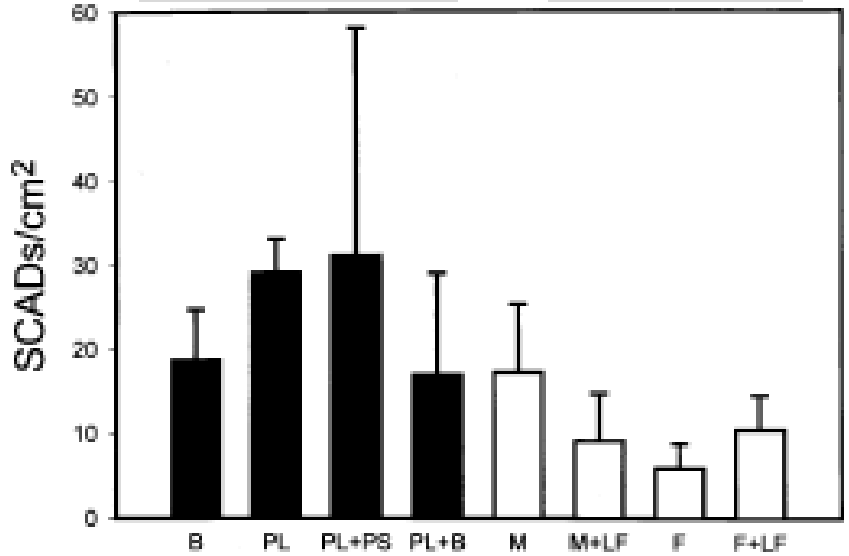


Fig 2. Mean SCAD density ± standard error by filter or cell saver group. Closed bars represent arterial filter group; open bars represent cell saver group. p < 0.05 for cell saver versus arterial filter groups; p > 0.05 for all other intergroup comparisons. (B = Bentley Duraflo II AF-1025D; PL = Pall LeukoGuard AL; PS = Pall StatPrime; M = Medtronic autoLog cell saver, LF = Pall RCXL 1 leukocyte removal filter; F = Fresenius Continuous autotransfusion System.)

Kincaid EH, Jones TJ, Stump DA, Brown WR, Moody DM, Deal DD, et al. Processing scavenged blood with a cell saver reduces cerebral lipid microembolization. Ann Thorac Surg. 2000;70(4):1296–300.

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5. Gestion des aspirations

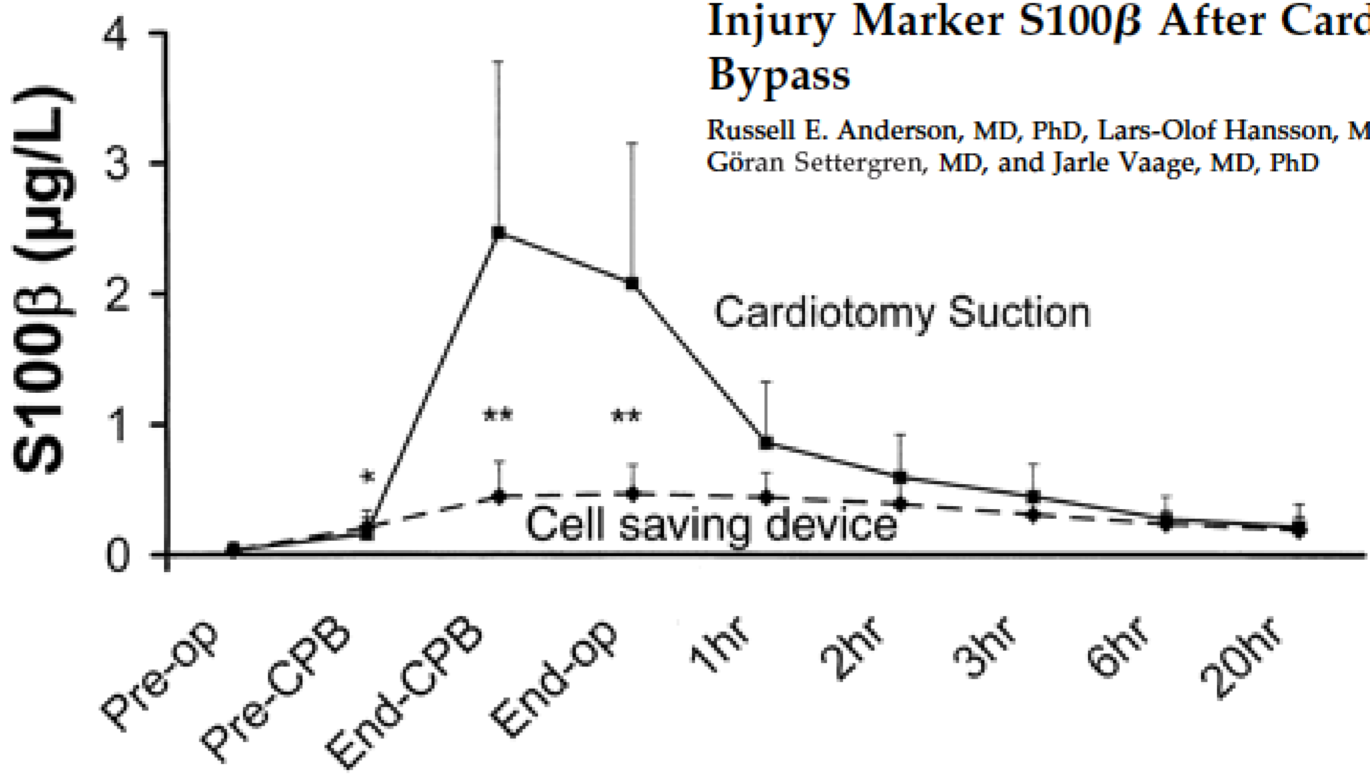
Cell-Saver et réponse inflammatoire

Réduction des concentrations circulantes:

- **hémoglobine libre** ***(Reents Ann Thorac Surg 1999)***
- **cytokines** ***(Reents Ann Thorac Surg 1999)***
- **protéine S100b** ***(Anderson Ann Thorac Surg 2000)***

The Effect of Cardiotomy Suction on the Brain Injury Marker S100β After Cardiopulmonary Bypass

Russell E. Anderson, MD, PhD, Lars-Olof Hansson, MD, PhD, Jan Liska, MD, PhD, Göran Settergren, MD, and Jarle Vaage, MD, PhD



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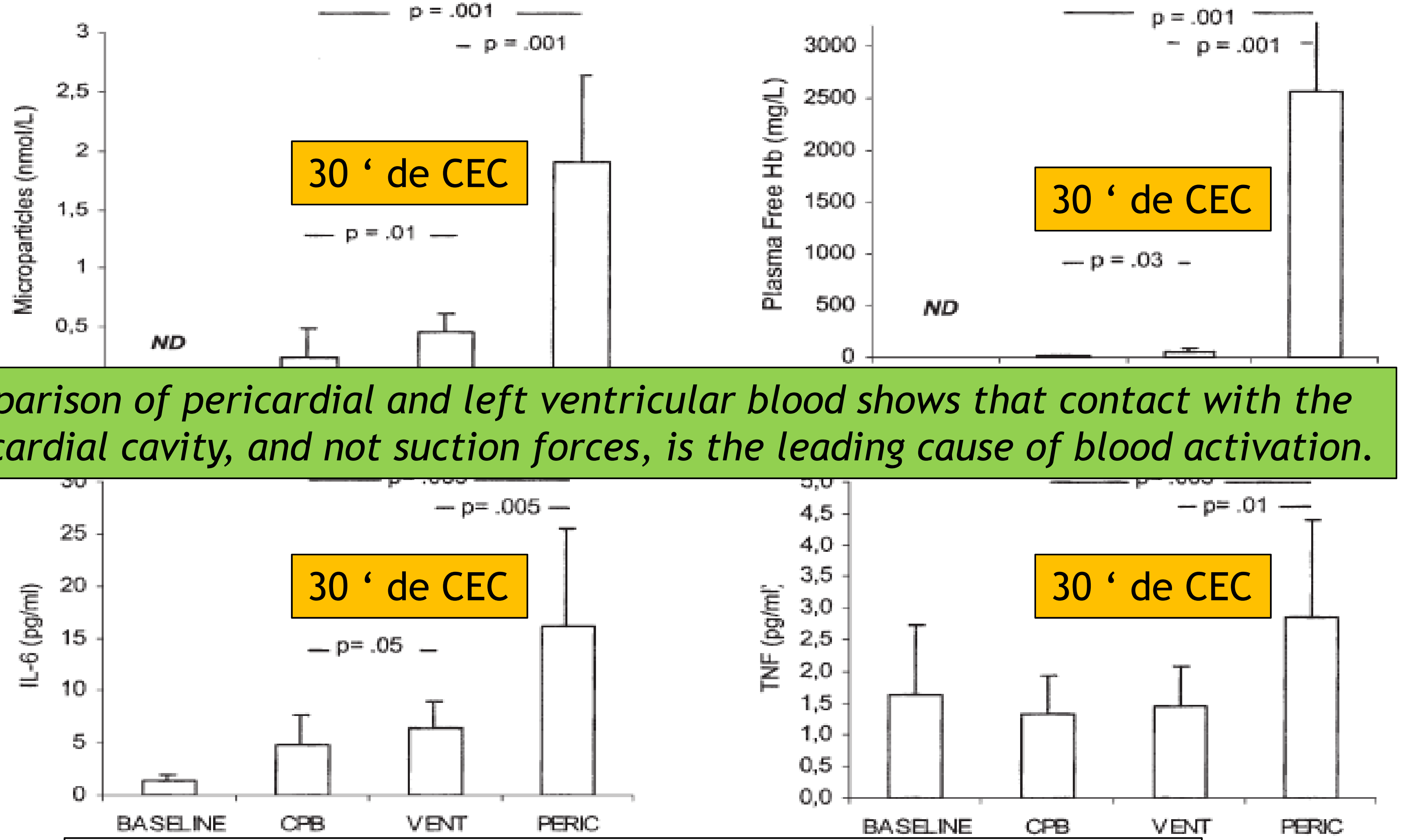
Source lipidique extra cérébrale de la protéine s100β (non spécifique)

7 patients (*Part II*)		s100β en µg/L
Champ opératoire	Incision cutanée	12 ± 5
	Après sternotomie	42 ± 18
Réservoir du cell-saver	Avant lavage	33 ± 12
	Après lavage	1,9 ± 0,9
Sérum	préopératoire	0,03 ± 0,04
	postopératoire	0,44 ± 0,17

Le recours à un *cell-saver* permet de limiter la transfusion de particules lipidiques à partir du champ opératoire

Anderson RE, Hansson LO, Liska J, Settergren G, Vaage J. The effect of cardiotomy suction on the brain injury marker S100beta after cardiopulmonary bypass. The Annals of Thoracic Surgery 2000;69:847–50.

Le péricarde comme source d'activation inflammatoire et d'hémolyse



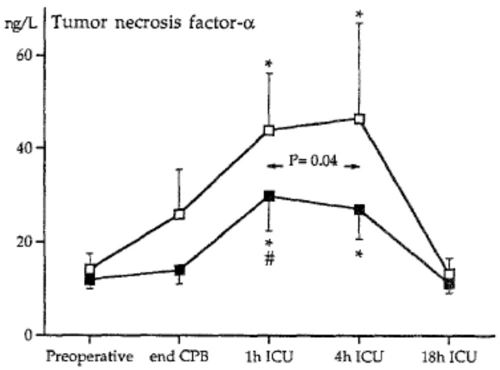
Comparison of pericardial and left ventricular blood shows that contact with the pericardial cavity, and not suction forces, is the leading cause of blood activation.

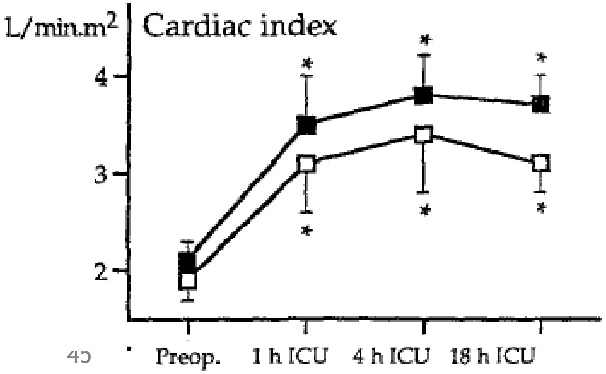
Fabre O, Vincentelli A, Corseaux D, Juthier F, Susen S, Bauters A, et al. Comparison of blood activation in the wound, active vent, and cardiopulmonary bypass circuit. The Annals of Thoracic Surgery 2008;86:537-41.

La production de TNF varie avec l'âge et altère la performance myocardique

MYOCARDIAL PERFORMANCE IN ELDERLY PATIENTS AFTER CARDIOPULMONARY BYPASS IS SUPPRESSED BY TUMOR NECROSIS FACTOR

<55 ans vs >65 ans





The aim of this study was to determine whether elderly patients (aged ≥65 years, $n = 20$) in comparison with younger patients (aged ≤55 years, $n = 23$) demonstrate a different biochemical and hemodynamic response to coronary artery bypass operations. In the elderly group, we calculated a smaller body surface area ($p < 0.01$) than that in the younger group, and more female patients were included in this group ($p < 0.05$). During cardiopulmonary bypass, the elderly had higher endotoxin plasma concentrations ($p < 0.01$) than the younger patients, and significantly more circulating tumor necrosis factor-alpha was found after operation ($p < 0.04$). In the intensive care unit, the elderly patients had a significantly higher pulmonary capillary wedge pressure ($p < 0.001$), a higher mean pulmonary artery pressure ($p < 0.01$), and a lower calculated left ventricular stroke work index ($p < 0.05$). Multivariate analysis for the postoperative outcome showed that the intergroup differences in tumor necrosis factor-alpha, mean pulmonary artery pressure, and pulmonary capillary wedge pressure could be explained mainly by the difference in age between the groups and that the calculated left ventricular stroke work index difference could be explained by the difference in circulating tumor necrosis factor-alpha levels. Thus in elderly patients higher circulating endotoxin and tumor necrosis factor-alpha concentrations were detected than in younger patients, which clinically resulted in a suppressed myocardial performance. (J THORAC CARDIOVASC SURG 1995;110:1663-9)

Henk te Velthuis, PhD,[a] Piet G. M. Jansen, MD, PhD,[a]
Heleen M. Oudemans-van Straaten, MD,[a] Augueste Sturk, PhD,[b]
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Velthuis H te, Jansen PGM, Straaten HMO, Sturk A, Eijsman L, Wildevuur CRH. Myocardial performance in elderly patients after cardiopulmonary bypass is suppressed by tumor necrosis factor. The Journal of Thoracic and Cardiovascular Surgery 1995;110:1663-9.

CHU ANGERS
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Hémolyse: la pompe ou les aspirations ?

standard roller pump (STD, n = 20),
dynamically set nonocclusive roller pump (DYN, n = 20)
centrifugal pump (CEN, n = 20).

La réinjection du sang des aspirations de cardiotomie est la principale source d'hémoglobine libre plasmatique

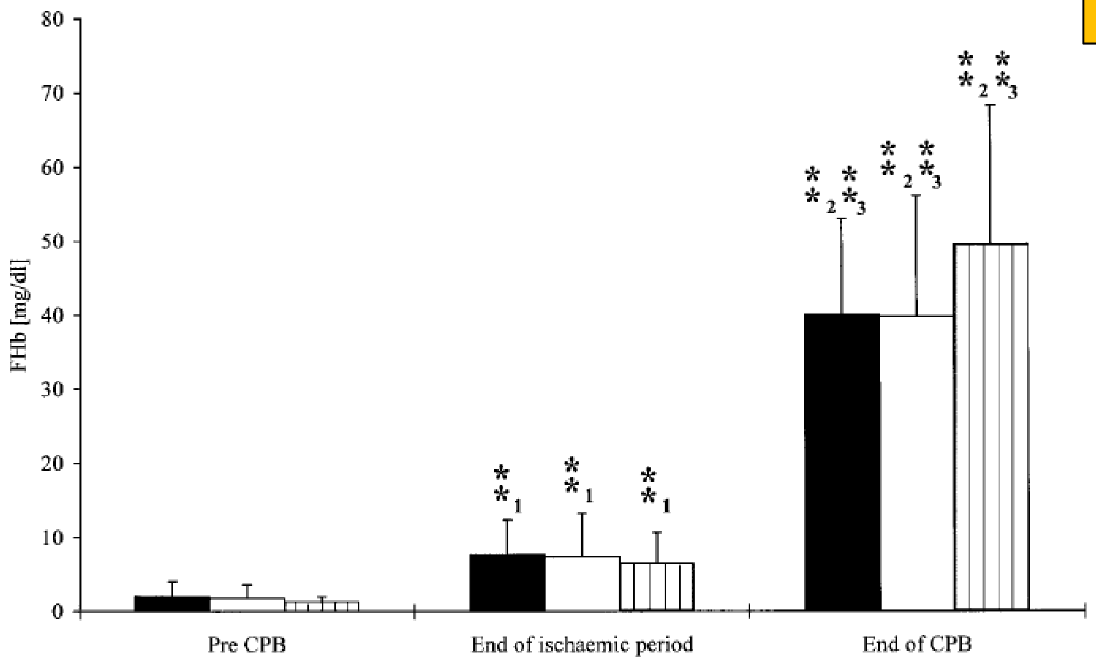

Figure 4 FHb, CEN group (solid bars), STD group (open bars) and DYN group (hatched bars). **1 $p < 0.001$ for all groups at the end of the ischaemic phase of CPB compared to pre-CPB, **2 $p < 0.001$ for all groups at the end of CPB compared to pre-CPB, **3 $p < 0.001$ for all groups at the end of CPB compared to the end of the ischaemic phase.

Hansbro SD, Sharpe DA, Catchpole R, Welsh KR, Munsch CM, McGoldrick JP, et al. Haemolysis during cardiopulmonary bypass: an in vivo comparison of standard roller pumps, nonocclusive roller pumps and centrifugal pumps. Perfusion. 1999;14(1):3-10.

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Qualité du sang récupéré
Aspirations de cardiotomie *vs* cell-saver

Table 1. Concentration of Proinflammatory Cytokines, Hemostasis Factors, Free Hemoglobin, Leukocyte Count, and Hematocrit

Variables	Patient Preop	Patient Intraop	Patient Postop	Cardiotomy Suction Intraop	avant Haem 1	après process Haem 2
IL-6 (μg/L)	2	10	113	52[a]	178	9
	(1–6)	(8–30)	(38–157)	(18–89)	(77–843)	(2–30)
IL-8 (μg/L)	13	20	29	26[a]	95	39[b]
	(10–19)	(16–29)	(20–43)	(24–42)	(54–106)	(27–43)
TNF-α (μg/L)	0	1	0	24[a]	22	0
	(0–4)	(0–5)	(0–2)	(20–33)	(0–33)	(0–0)
TAT (μg/L)	5	43	81	113[a]	693	137[b]
	(3–15)	(32–73)	(40–108)	(99–153)	(586–870)	(20–313)
PAP (μg/L)	427	489	653	566[a]	899	20
	(285–505)	(393–607)	(496–773)	(505–658)	(644–965)	(14–34)
Thrombocytes ($10^3/\mu L$)	195	137	124	127	60	14
	(154–220)	(123–158)	(113–151)	(114–144)	(49–66)	(11–17)
$CD62^+$	3	6	28	2	NA	NA
Thrombocytes (%)	(0–4)	(1–13)	(7–46)	(1–6)		
Free Hb (mg/dL)	24	30	38	61[a]	500	58[b]
	(18–34)	(27–32)	(31–43)	(50–70)	(342–652)	(45–62)
Leukocytes ($10^3/\mu L$)	4.6	7.1	9.6	6.0	3.7	5.2
	(4.0–6.1)	(5.2–8.9)	(8.9–12.0)	(4.8–8.0)	(2.8–4.0)	(3.4–6.3)
Hematocrit (%)	37.5	23.1	25.3	23	16	28.8
	(35.3–40.4)	(21.7–24.3)	(24.5–26)	(21.6–23.3)	(12.7–19.3)	(24.1–29.1)

[a] Value significantly different from patients intraop value; [b] Value above the reference range in the processed blood.

Data are presented as medians with the lower and upper quartiles in parentheses.

Patient preop, intraop, and postop samples taken from the arterial catheter in the course of the operation.

Cardiotomy suction intraop samples taken from the cardiotomy suction. Haem 1 and Haem 2 samples taken from blood collected with the Haemonetics system before (Haem 1) and after processing (Haem 2).

Hb = hemoglobin; IL = interleukin; NA = not analyzed; PAP = plasmin-antiplasmin complex; TAT = thrombin-antithrombin complex; TNF-α = tumor necrosis factor-α.

Réduction paramètres

- SIRS Cytokines
- Coagulation
- Fibrinolyse
- Hémolyse

Contamination bactérienne:

- Fréquente 90%
- Faible charge (<10/mL)

Reents W, Babin-Ebell J, Misoph MR, Schwarzkopf A, Elert O. Influence of different autotransfusion devices on the quality of salvaged blood. The Annals of Thoracic Surgery 1999;68:58-62.

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Qualité du sang récupéré au cell-saver
Contamination bactérienne

Table I. *Bacterial and endotoxin assay of patient and Cell Saver System blood and priming fluid during cardiac operations*

	Bacterial cultures	*Endotoxin assay*
	No. positive/No. of tests (%)	*No. positive/No. of tests (%)*
Blood		
Preoperative	4/37 (10.8)	0/35 (0)
Intraoperative	11/36 (30.6)	5/35 (14.3)
Cell Saver System	30/31 (96.8)	7/29 (24.1)
Postoperative	1/28 (3.6)	5/25 (20)
All blood	46/132 (34.8)	17/124 (13.7)
Priming fluid	0/38 (0)	0/35 (0)
Total	46/169 (27.2)	17/159 (10.7)

- Etude prospective chez 38 patients
- Contamination bactérienne du réservoir de cell-saver fréquente
- Germes contaminants en provenance de l'air ambiant, de la flore cutanée, ou des surfaces environnementales
- 79,5% staph. coag. neg. et 20,5% diphtéroïdes
- Aucun épisode de sepsis postopératoire

Bland LA, Villarino ME, Arduino MJ, McAllister SK, Gordon SM, Uyeda CT, et al. Bacteriologic and endotoxin analysis of salvaged blood used in autologous transfusions during cardiac operations. J Thorac Cardiovasc Surg 1992;103:582–8.

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Hemodynamic effects of cardiotomy suction blood

Martin Westerberg, MD, PhD,[a] Jakob Gäbel, MD,[a] Anders Bengtsson, MD, PhD,[b] Johan Sellgren, MD, PhD,[c] Ola Eidem, ECCP,[a] and Anders Jeppsson, MD, PhD[a]

Dr Westerberg

J Thorac Cardiovasc Surg 2006;131:1352-7

Objective: Cardiac surgery induces a systemic inflammatory activation, which in severe cases is associated with peripheral vasodilation and hypotension. Cardiotomy suction blood contains high levels of inflammatory mediators, but the effect of cardiotomy suction blood on the vasculture is unknown. We investigated the effect of cardiotomy suction blood on systemic vascular resistance in vivo and whether cell-saver processing of suction blood affects the vascular response.

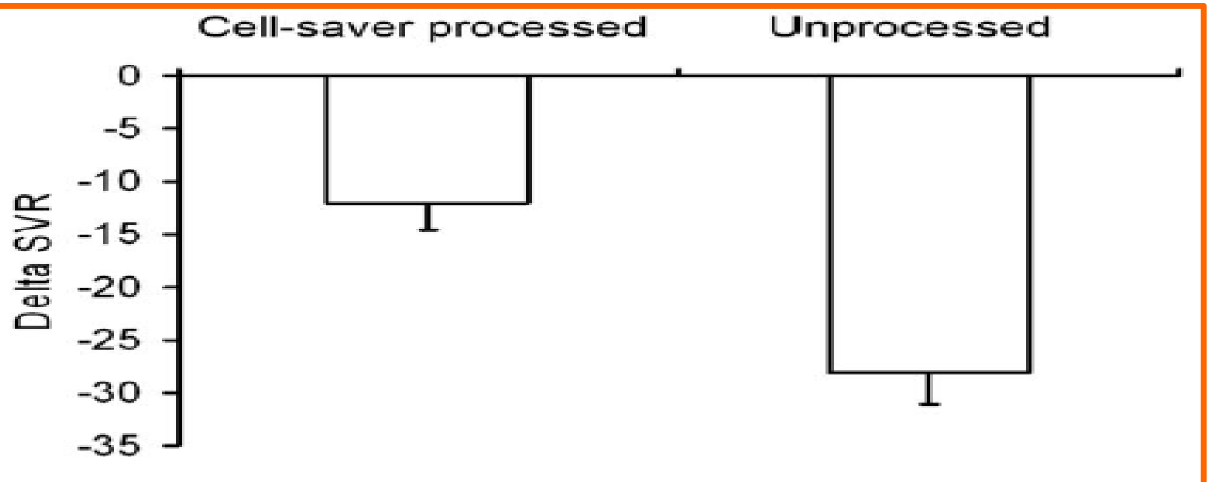

Figure 2. Relative changes in systemic vascular resistance (*SVR*) during retransfusion of cell-saver processed or cell-saver unprocessed cardiotomy suction blood (mean ± standard error of the mean). There was a significant difference between the 2 groups ($P = .001$).

Conclusions: The results suggest cardiotomy suction blood is vasoactive and might influence vascular resistance and blood pressure during cardiac surgery. The observed vasodilation is proportional to the inflammatory activation of suction blood and can be reduced by processing suction blood with a cell-saving device before retransfusion.

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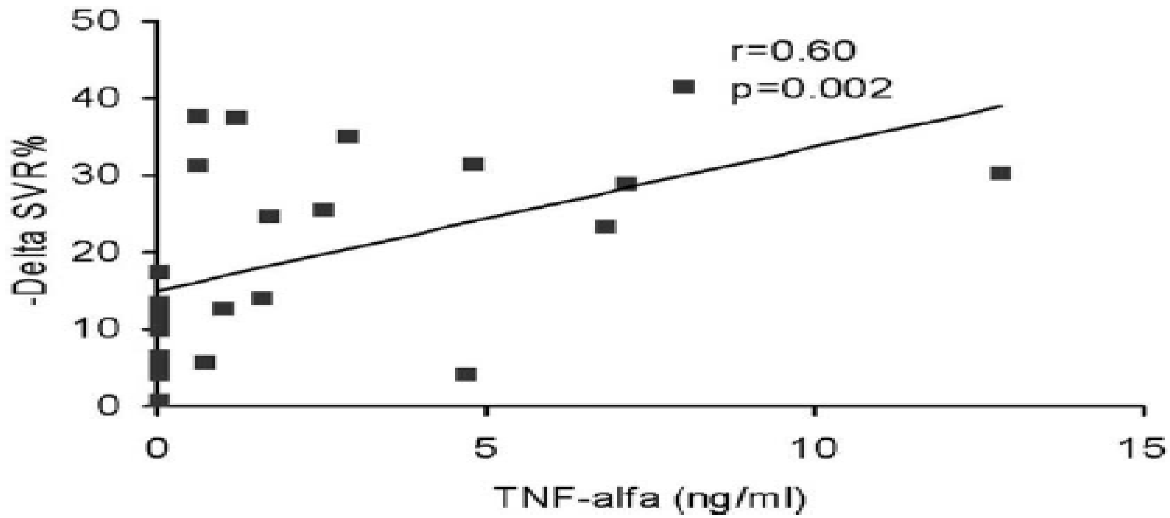
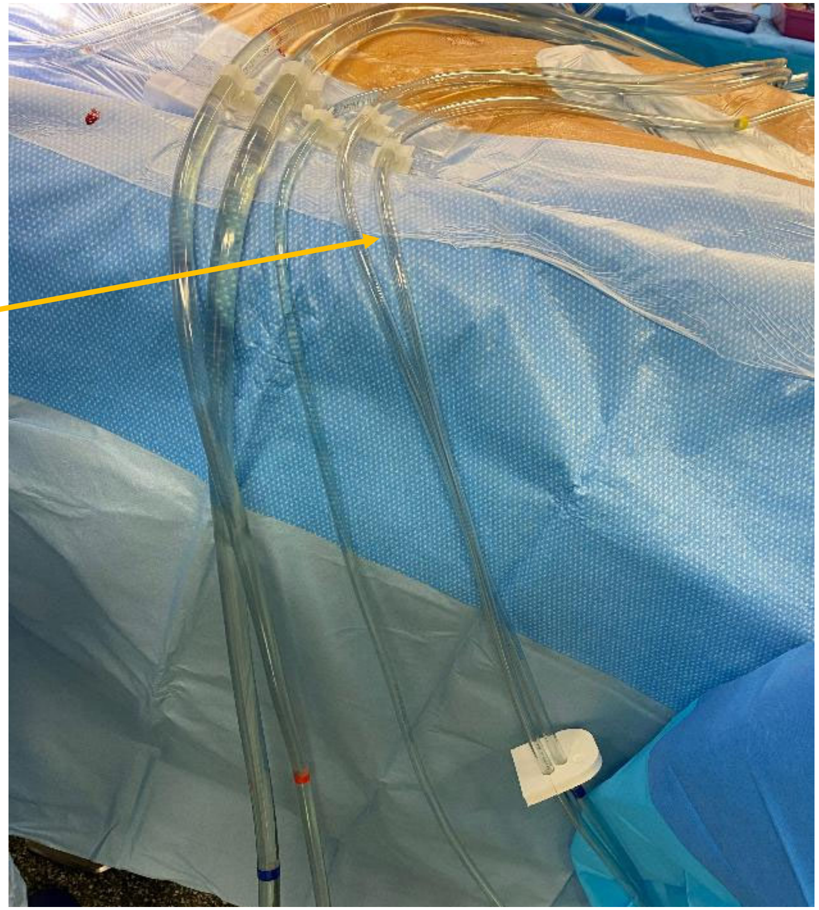


Figure 3. Correlation between plasma levels of TNF-α in retransfused cardiotomy suction blood and relative changes in systemic vascular resistance.

Conclusions: The results suggest cardiotomy suction blood is vasoactive and might influence vascular resistance and blood pressure during cardiac surgery. The observed vasodilation is proportional to the inflammatory activation of suction blood and can be reduced by processing suction blood with a cell-saving device before retransfusion.

En pratique comment faire ?

- Utiliser systématiquement un cell-saver
- Conserver l'installation de la ligne d'aspiration de cardiotomie en place (*rescue*)
- Dans l'urgence, se souvenir que si le sang aspiré n'a séjourné que quelques secondes dans le péricarde, il n'a pas eu le temps de subir une activation importante
- Le sang de la décharge VG n'est pas soumis à la même activation



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6. Traitements de surfaces

Standard CPB +
Cardiotomy suction

Heparin-coated CPB +
Cardiotomy suction

Heparin-coated CPB
No cardiotomy suction

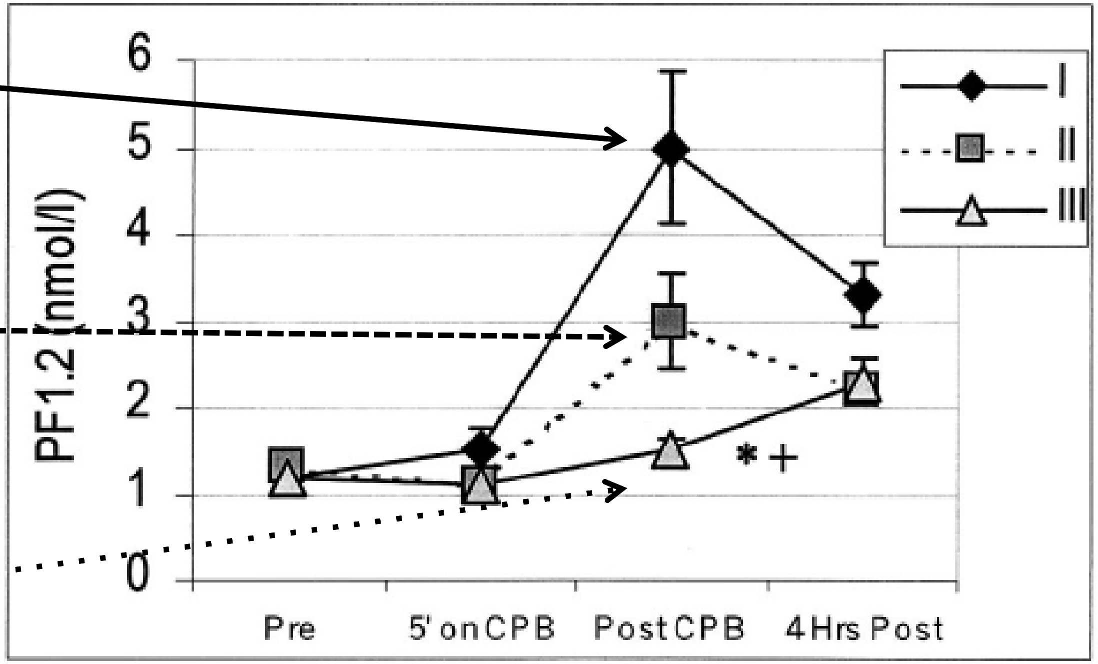
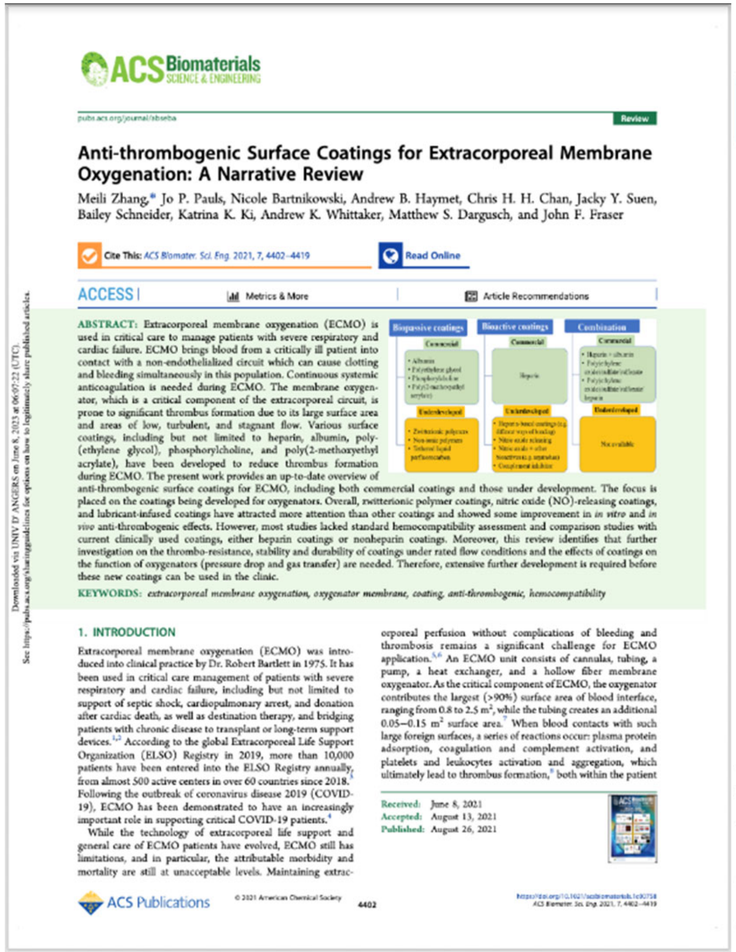


Figure 1. Comparison of thrombin generation (PF-1.2) for different treatment strategies. *Diamonds,* Group I; *squares,* group II; *triangles,* group III. *Asterisk* indicates *P* < .001 for group I versus group III; *plus sign* indicates *P* = .042 for group II versus group III, by ANOVA and Scheffé test.

ACT @ 450s using Hepcon® HMS

Aldea GS et al. Limitation of thrombin generation, platelet activation, and inflammation by elimination of cardiotomy suction in patients undergoing coronary artery bypass grafting treated with heparin-bonded circuits. J Thorac Cardiovasc Surg 2002;123(4):742-55.

6. Traitements de surfaces



ACS Biomaterials Science & Engineering
pubs.acs.org/journal/abseba Review

Anti-thrombogenic Surface Coatings for Extracorporeal Membrane Oxygenation: A Narrative Review

Meili Zhang,* Jo P. Pauls, Nicole Bartnikowski, Andrew B. Haymet, Chris H. H. Chan, Jacky Y. Suen, Bailey Schneider, Katrina K. Ki, Andrew K. Whittaker, Matthew S. Dargusch, and John F. Fraser

Cite This: *ACS Biomater. Sci. Eng.* 2021, 7, 4402−4419 Read Online

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ABSTRACT: Extracorporeal membrane oxygenation (ECMO) is used in critical care to manage patients with severe respiratory and cardiac failure. ECMO brings blood from a critically ill patient into contact with a non-endothelialized circuit which can cause clotting and bleeding simultaneously in this population. Continuous systemic anticoagulation is needed during ECMO. The membrane oxygenator, which is a critical component of the extracorporeal circuit, is prone to significant thrombus formation due to its large surface area and areas of low, turbulent, and stagnant flow. Various surface coatings, including but not limited to heparin, albumin, poly(ethylene glycol), phosphorylcholine, and poly(2-methoxyethyl acrylate), have been developed to reduce thrombus formation during ECMO. The present work provides an up-to-date overview of anti-thrombogenic surface coatings for ECMO, including both commercial coatings and those under development. The focus is placed on the coatings being developed for oxygenators. Overall, zwitterionic polymer coatings, nitric oxide (NO)-releasing coatings, and lubricant-infused coatings have attracted more attention than other coatings and showed some improvement in *in vitro* and *in vivo* anti-thrombogenic effects. However, most studies lacked standard hemocompatibility assessment and comparison studies with current clinically used coatings, either heparin coatings or nonheparin coatings. Moreover, this review identifies that further investigation on the thrombo-resistance, stability and durability of coatings under rated flow conditions and the effects of coatings on the function of oxygenators (pressure drop and gas transfer) are needed. Therefore, extensive further development is required before these new coatings can be used in the clinic.

KEYWORDS: *extracorporeal membrane oxygenation, oxygenator membrane, coating, anti-thrombogenic, hemocompatibility*

1. INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) was introduced into clinical practice by Dr. Robert Bartlett in 1975. It has been used in critical care management of patients with severe respiratory and cardiac failure, including but not limited to support of septic shock, cardiopulmonary arrest, and donation after cardiac death, as well as destination therapy, and bridging patients with chronic disease to transplant or long-term support devices.[1,2] According to the global Extracorporeal Life Support Organization (ELSO) Registry in 2019, more than 10,000 patients have been entered into the ELSO Registry annually, from almost 500 active centers in over 60 countries since 2018.[3] Following the outbreak of coronavirus disease 2019 (COVID-19), ECMO has been demonstrated to have an increasingly important role in supporting critical COVID-19 patients.[4]

While the technology of extracorporeal life support and general care of ECMO patients have evolved, ECMO still has limitations, and in particular, the attributable morbidity and mortality are still at unacceptable levels. Maintaining extracorporeal perfusion without complications of bleeding and thrombosis remains a significant challenge for ECMO application.[5,6] An ECMO unit consists of cannulas, tubing, a pump, a heat exchanger, and a hollow fiber membrane oxygenator. As the critical component of ECMO, the oxygenator contributes the largest (>90%) surface area of blood interface, ranging from 0.8 to 2.5 m^2, while the tubing creates an additional 0.05−0.15 m^2 surface area.[7] When blood contacts with such large foreign surfaces, a series of reactions occur: plasma protein adsorption, coagulation and complement activation, and platelets and leukocytes activation and aggregation, which ultimately lead to thrombus formation,[8] both within the patient

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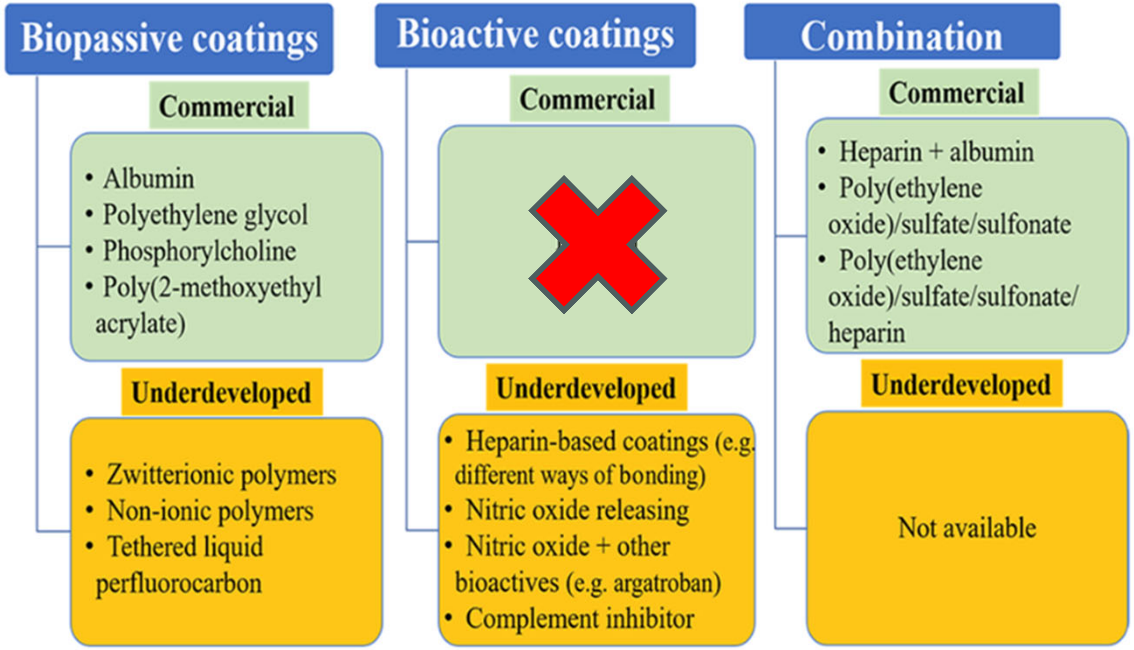

Figure 1. Overview of currently commercial and underdeveloped anti-thrombogenic surface coatings for ECMO. These coatings can be categorized as bioactive coatings, biopassive coatings, and their combination.

Zhang, M. *et al*. Anti-thrombogenic Surface Coatings for Extracorporeal Membrane Oxygenation: A Narrative Review. *ACS Biomater. Sci. Eng.* **7**, 4402–4419 (2021).

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6. Traitements de surfaces

Alternatives aux heparin-coatings

The International Journal of Artificial Organs / Vol. 27 / no. 4, 2004 / pp. 311-319

Artificial Heart and Cardiac Assist Devices

Reduced systemic heparin dose with phosphorylcholine coated closed circuit in coronary operations

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[1] Departments of Cardiothoracic Anesthesia and
[2] Cardiac Surgery, Istituto Policlinico S. Donato Cardiovascular Center "E. Malan", University of Milan, Milan - Italy

ABSTRACT: In this prospective cohort study we addressed the clinical impact of a reduced anticoagulation protocol on the hospital outcome of patients undergoing coronary revascularization with cardiopulmonary bypass.
364 consecutive low to moderate risk patients scheduled for elective isolated coronary operations were admitted to the study. 184 patients (Control Group) received conventional open circuits and full systemic anticoagulation (target activated clotting time 480 seconds); 180 patients (Intraoperative ECMO group) received closed, phosphorylcholine coated circuits and a reduced systemic heparin dose (target activated clotting time 320 seconds).
Patients of the Intraoperative ECMO group had less requirement for allogeneic blood products (odds ratio 0.55, 95% confidence interval 0.34-0.92, p= 0.02), a significant containment of blood loss (374 ± 278 mL vs. 463 ± 321 mL in Control group, p= 0.005) a lower postoperative peak serum creatinine levels (1.19 ± 0.48 mg/dL vs. 1.41 ± 0.94 mg/dL in Control group, p= 0.048), and a significant lower rate of severe morbidity (odds ratio 0.27, 95% confidence interval 0.09-0.81, p= 0.02). A reduction of systemic anticoagulation is feasible with a non-heparin-bonded, closed biocompatible circuit, and results in a significant improvement of the outcome of low to moderate risk coronary patients. (Int J Artif Organs 2004; 27: 311-9)

KEY WORDS: Cardiopulmonary bypass, Coronary artery bypass surgery, Heparin, Database, Complications of surgery

INTRODUCTION

Previous studies have demonstrated that the use of "tip-to-tip" heparin-bonded circuits with a lower anticoagulation protocol results in significant improvement of the postoperative outcome of patients undergoing coronary artery bypass graft (CABG) surgery with cardiopulmonary bypass (CPB) (1-4). An accurate analysis of the separate effects of heparin-bonding and reduction of systemic heparinization (4) indicated that the latter was the main determinant of a reduction in homologous blood requirements, thromboembolic complication rate, and decreased length of hospital stay. This conclusion supports the evidence that simply using a heparin-coated circuit does not induce a major improvement in the postoperative course (5) other than in selected populations of high-risk patients (6) or when limited to subclinical lung function improvements (7, 8). Conversely, in a recent study, Øvrum and coworkers (9) demonstrated that the routine application of a low systemic anticoagulation protocol determines a rapid recovery after CABG operations, with a minimal complication rate.

In a recent paper (10) we were able to demonstrate that by using a non-heparin bonded, low thrombogenic circuit based on a phosphorylcholine coating, applied to a totally closed CPB circuit, a reduction of systemic heparinization was feasible and safe, and that the results in terms of clinical coagulation tests and postoperative outcome were similar to those obtained using a heparin-bonded circuit with a similar reduced anticoagulation protocol (9). As our circuit and coagulation management is very similar to the one commonly used for long-term ExtraCorporeal

 0391-3988/311-09 $15.00/0

Interactive CardioVascular and Thoracic Surgery 18 (2014) 763–769
doi:10.1093/icvts/ivu011 Advance Access publication 14 March 2014

ORIGINAL ARTICLE – ADULT CARDIAC

An *ex vivo* evaluation of blood coagulation and thromboresistance of two extracorporeal circuit coatings with reduced and full heparin dose†

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ORIGINAL ARTICLE

Abstract

OBJECTIVES: Bioactive Carmeda® heparin-coated extracorporeal circuits (ECCs) have been shown to reduce contact phase and coagulation activation during cardiopulmonary bypass (CPB). Heparin coating is therefore effective in safely reducing coagulation during routine CPB. Balance® Biosurface is a new, recently developed biopassive coating containing negatively charged sulphonated polymers. This study sought to compare the clotting activation and thromboresistance of the Balance® (B) circuit with that of the Carmeda® (C) with full-dose systemic heparin (FDH) and reduced-dose systemic heparin (RDH).

METHODS: This *ex vivo* study set-up comprising 40 experiments consisted of simplified ECC and circulation of freshly donated human blood. RDH and FDH regimens were obtained with 0.5 IU/ml and 1 IU/ml heparin administered to reach target activated clotting times (ACTs) of 250 and 500 s, respectively. The study design comprised four groups: FDH-C, FDH-B, RDH-C and RDH-B (all $n = 10$). Blood was sampled prior to and during the 2-h CPB. Coagulation activation was assessed (FXIIa, F1.2) and electron microscope scan imaging of oxygenators enabled determination of adhesion scores.

RESULTS: With a biopassive compared with bioactive surface, mean ACT was lower, regardless of the heparin regimen applied ($P < 0.001$), whereas the total heparin dose required to maintain ACT was above target level ($P < 0.001$). However, FXIIa and F1.2 values were similar in all groups throughout, as were pressure gradients among oxygenators. All groups demonstrated similar adhesion scores following ultrastructural oxygenator assessment.

CONCLUSIONS: In the absence of surgical-related haemostatic disturbances and based on target ACT levels under reduced- or full-dose heparin, the clotting process was similar to heparin-coated and new sulphonated polymer-coated ECC, both demonstrating similar thromboresistance.

Keywords: Cardiopulmonary bypass • Surface coating • Thromboresistance • Coagulation

INTRODUCTION

Cardiopulmonary bypass (CPB) causes coagulation activation when blood comes into contact with artificial surfaces. To avoid circuitry blood clotting and thromboembolic complications, systemic heparin is administered to both the patient and circuits, in line with protocols laid down in the 70 s [1, 2]. Standard practice dictates that 300 IU/kg heparin be associated with 5000 IU in the prime volume, despite this practice being based on weak evidence regarding appropriate patient anticoagulation. Some authors have, in fact, reported that this full-dose anticoagulation approach unnecessarily exposes the patient to excessive blood loss [3]. On the other hand, safe, low systemic anticoagulation protocols have been developed utilizing a comprehensive strategy comprising biocompatible closed circuits, retrograde autologous prime, routine use of cell saver, antifibrinolytics and dedicated point-of-care devices for determining adequate heparin and protamine doses [4-6]. Of all biocompatible circuits, Bioactive Carmeda® heparin coating is currently the most available having undergone extensive assessment in a low systemic anticoagulation setting [7, 8]. This strategy produced a very satisfactory clinical outcome with no signs of clotting [8], also offering the possibility of alleviating clopidogrel-related complications in patients undergoing coronary artery bypass grafting [9].

†Presented at the 27th Annual Meeting of the European Association for Cardio-Thoracic Surgery, Vienna, Austria, 5–9 October 2013.

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Biopassif vs Bioactif

- **Duraflo II** vs **Phisio**
- 100 UI/Kg vs 150 UI/Kg
- ACT @ 300s vs ACT @ 320s

The International Journal of Artificial Organs / Vol. 25 / no. 9, 2002 / pp. 875-881

Artificial Heart and Cardiac Assist Devices

Closed, phosphorylcholine-coated circuit and reduction of systemic heparinization for cardiopulmonary bypass: The intraoperative ECMO concept

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[1] Departments of Cardiot
[2] Cardiovascular Perfusic
Italy

ABSTRACT: Cardiopulmonary bypass with heparin-bonded circuits reduces systemic heparinization which is associated to a better clinical outcome in cardiac operations. In the present study, a novel biocompatible treatment, based on a phosphorylcholine coating without heparin, has been used to reduce systemic heparinization during cardiopulmonary bypass. Sixty patients underwent coronary revascularization with a fully phosphorylcholine-coated circuit. The circuit was entirely closed; suctions from the field were separated during the cardiopulmonary bypass time. A low systemic heparinization protocol based on half the loading dose of heparin (150 IU/kg) and a target activated clotting time of 320 seconds was applied. No thrombus formation inside the extracorporeal circulation circuit occurred; in-hospital mortality was absent. One patient (1.6%) had a postoperative myocardial infarction and 2 (3.3%) were surgically revised due to bleeding. Homologous blood transfusion rate was 11.6%, postoperative bleeding was 310 ± 136 ml. If compared to patients treated with heparin-coated circuits and low systemic heparinization, these patients have better platelet count preservation and lower postoperative bleeding. The low thrombogenicity of phosphorylcholine-treated surfaces, despite the absence of surface-immobilized heparin, allows a safe reduction of systemic heparinization in the setting of an ECMO-like intraoperative cardiopulmonary - bypass. This intraoperative ECMO approach offers promising results in terms of clinical outcome after coronary revascularization operations. (Int J Artif Organs 2002; 25: 875-81)

INTRODUCTION

Heparin-bonded ci
cardiopulmonary bypass
mid '80s. They have a w
complement activation
cascade (1-3); from the
pulmonary complications
after coronary artery by
high-risk patients underg
associated with shorter
hospital stay, and with a
pulmonary and renal dys

7. Lutte contre hémodilution

- Provoque une augmentation de l'ACT non liée à l'héparinisation
- Contribue aux déperditions sanguines et au risque transfusionnel
- Majore le risque d'AVC *(Karkouti K et al Ann Thorac Surg 2005;80(4):1381-7)*
- Majore le risque d'IRA *(Karkouti K et al J Thorac Cardiovasc Surg 2005;129(2):391-400)*
- Attention au remplissage excessif préopératoire

Recourir aux techniques de priming rétrograde autologue pour éliminer autant que possible le volume d'amorçage de la CEC

Recommendations	Class[a]	Level[b]
Implementation of institutional measures to reduce haemodilution by fluid infusion and CPB during cardiac surgery to reduce the risk of bleeding and the need for transfusions is recommended.	I	C

Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA), Boer C, Meesters MI, Milojevic M, Benedetto U, Bolliger D, et al. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. J Cardiothorac Vasc Anesth. 2018 Feb;32(1):88-120.

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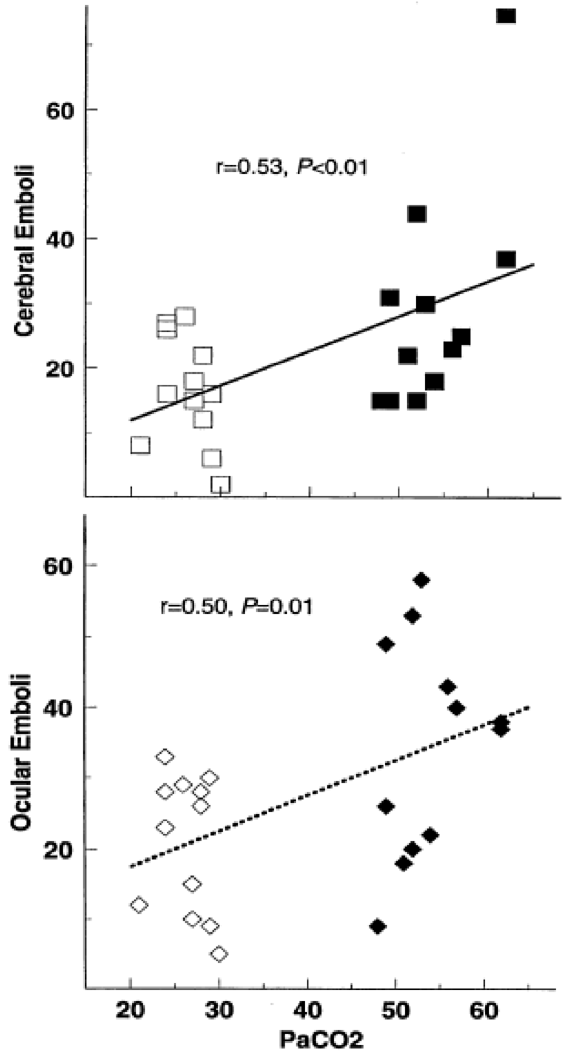
8. Limiter l'utilisation du CO2

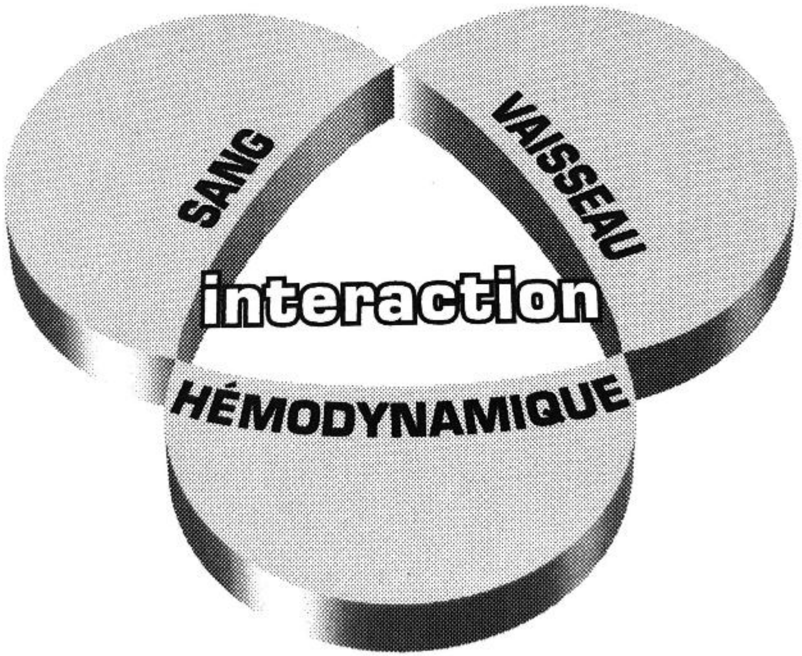
- Utilisé lors des purges cavitaires pour diminuer les embolies gazeuses
- **MAIS:**
  - → Induit une acidose
  - → Diminue les propriétés anticoagulantes de l'héparine
  - ➢ **Augmente le risque thrombotique**
  - → Provoque une vasodilatation cérébrale
  - ➢ **Augmente le risque embolique cérébral**



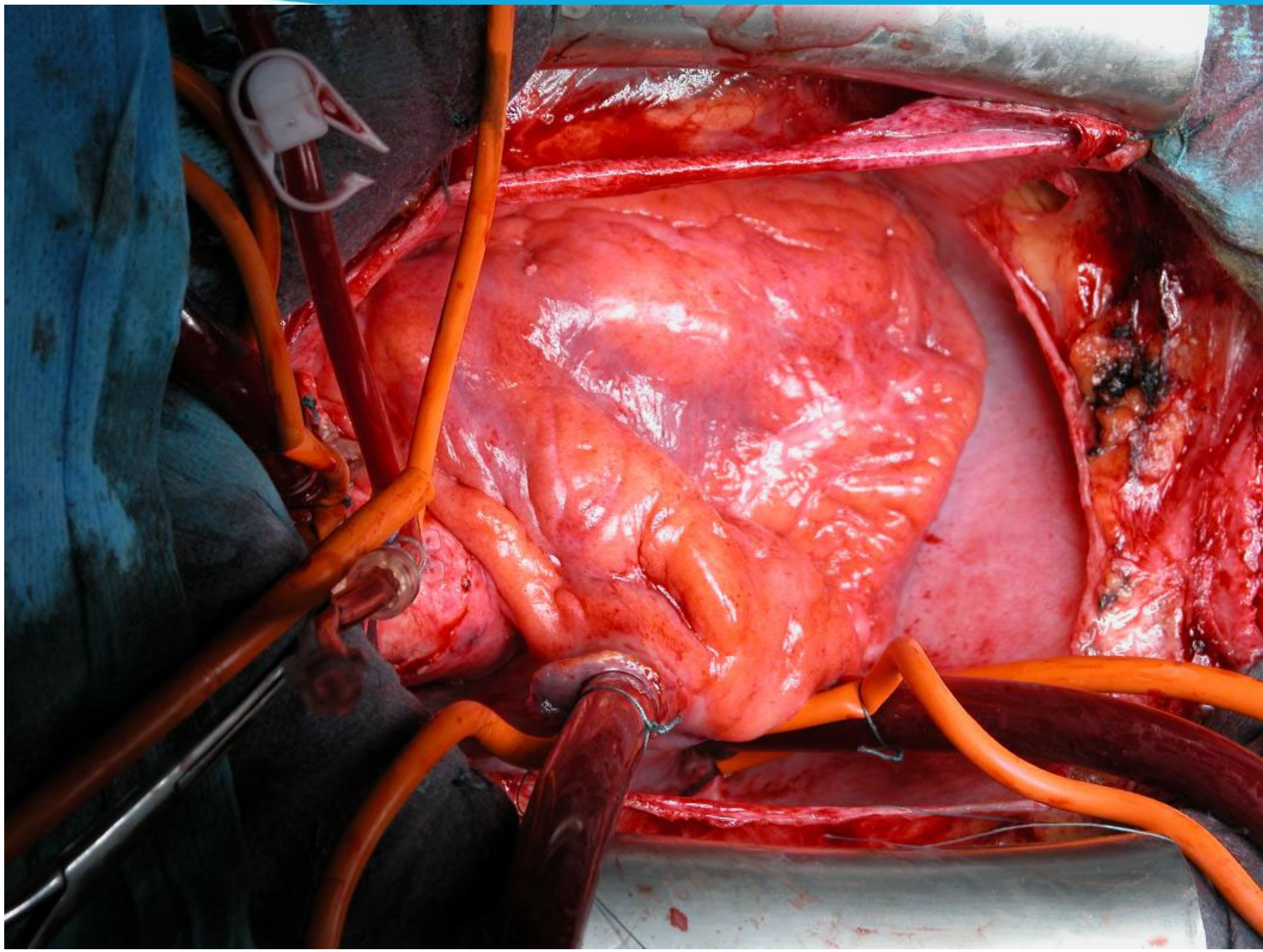
Cook DJ et al. Effect of temperature and PaCO2 on cerebral embolization during cardiopulmonary bypass in swine.. Ann Thorac Surg 2000;69(2):415-20.

9. Eviter la stagnation sanguine

Triade de Virchow



10. Hémostase chirurgicale rigoureuse



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Complications?

Existe-t-il un risque de morbidité lié à la réduction de l’héparine ou de l’anticoagulation ?

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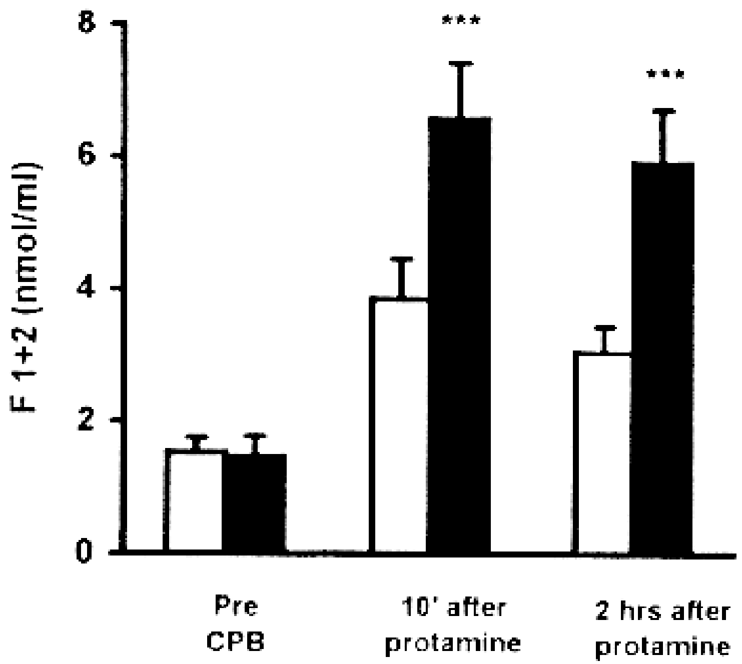
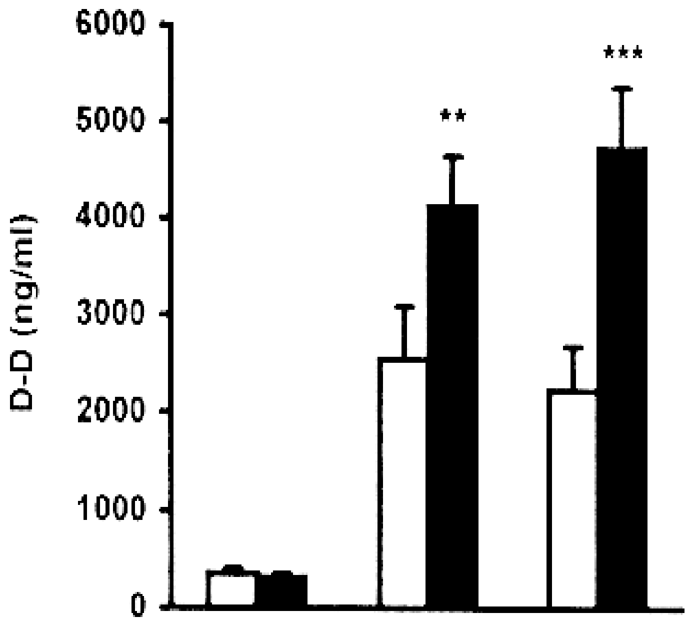
Réduction de l'anticoagulation sans gestion des aspirations

Réintroduction du sang activé dans la CEC !

Thrombin generation



Fibrinolytic activity



white bars: uncoated + full heparinization

black bars: coated + low heparinization

Kuitunen AH et al. Cardiopulmonary bypass with heparin-coated circuits and reduced systemic anticoagulation. Ann Thorac Surg 1997;63(2):438-44.

Surtout ne pas croire qu'un ACT très élevé protège de l'activation de la coagulation

Off-Pump Coronary Artery Bypass Operation Does Not Increase Procoagulant and Fibrinolytic Activity: Preliminary Results

Lars Englberger, MD, Franz F. Immer, MD, Friedrich S. Eckstein, MD, Pascal A. Berdat, MD, Andre Haeberli, PhD, and Thierry P. Carrel, MD

1. ACT 250 s in off-pump
2. ACT 480 s in uncoated CPB (32° C) with cardiotomy suction return: ACT at 692 s after heparin and >1000s during CPB

Augmenter l'ACT ne protège **pas en l'absence de gestion des aspirations** de l'augmentation de la thrombine circulante

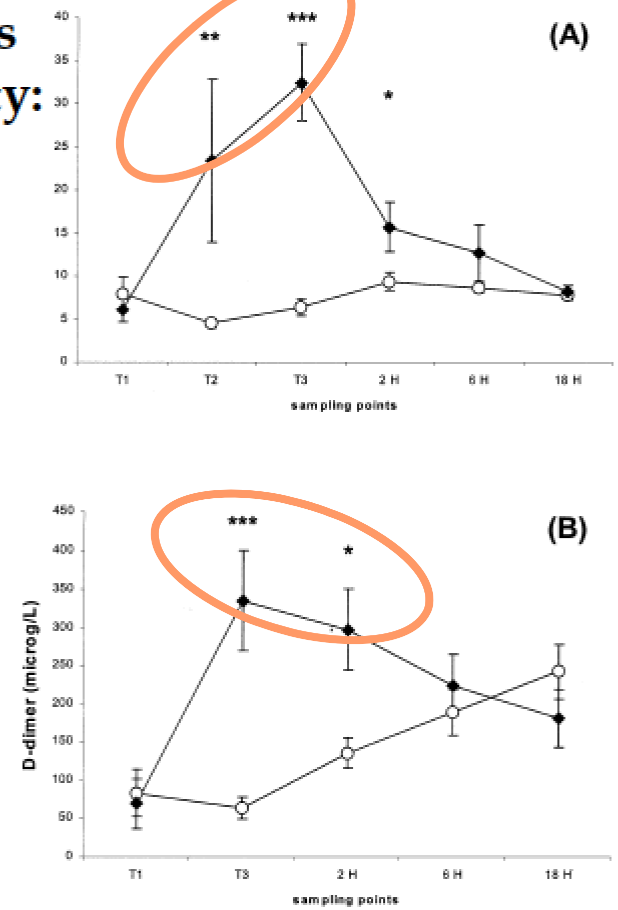


*Fig 3. (A) Thrombin-antithrombin complex (TAT [ANOVA p < 0.01]). (B) D-dimer (ANOVA p < 0.0001). Values shown not corrected for hemodilution. Data are presented as mean ± SEM. Significant intergroup differences (*p < 0.05; **p < 0.01; ***p < 0.001). Circles = off-pump group; diamonds = on-pump group. (ANOVA = analysis of variance; H = hours postoperative; T1 = baseline; T2 = during operation; T3 = end of operation.)*

Quelle est la place du ‘’moins d’héparine’’ dans les suites ?

Ou est-ce juste l’approche multifactorielle qui rend cette stratégie efficace ?

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Simple réduction de l'héparine
Repenser ses pratiques

Patients receiving lower dose of heparin has lower postoperative blood loss. The added benefit of significant drop in postoperative blood loss is evident.

- 20% p=0.0039

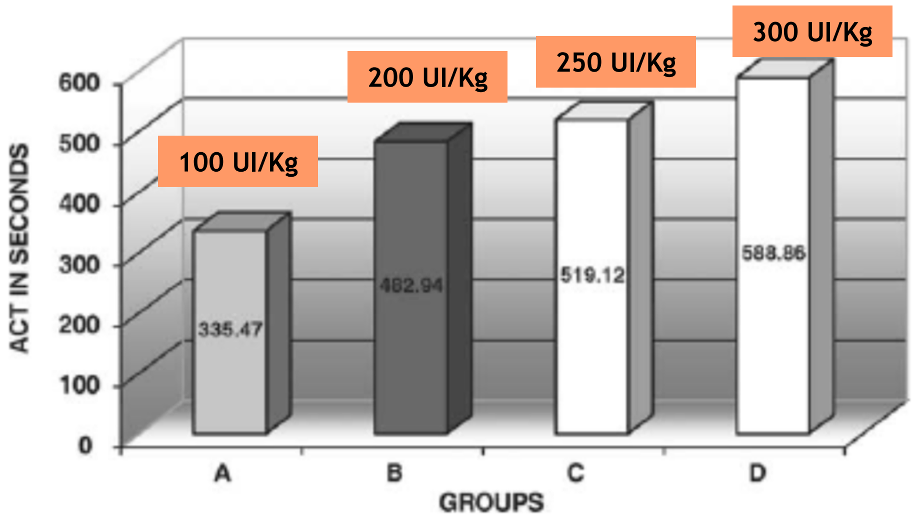

Fig. 2. Mean ACT after the initial dose of heparin in different groups.

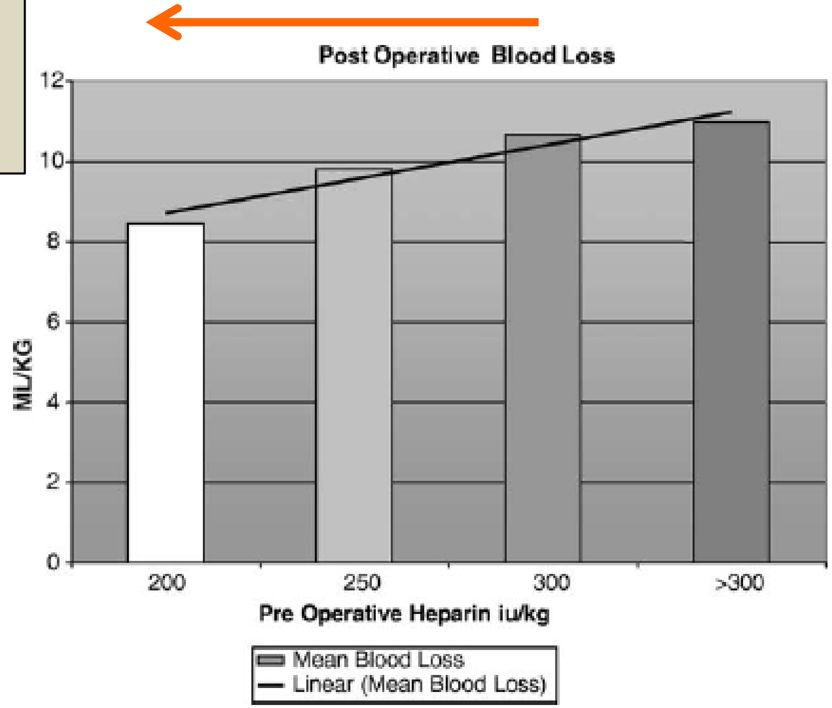

Fig. 3. Mean postoperative blood loss in millilitre per kilogram of patients receiving different preCPB heparin doses.

Shuhaibar MN, et al. How much heparin do we really need to go on pump? A rethink of current practices. Eur J Cardiothorac Surg. 2004;26(5):947-50.

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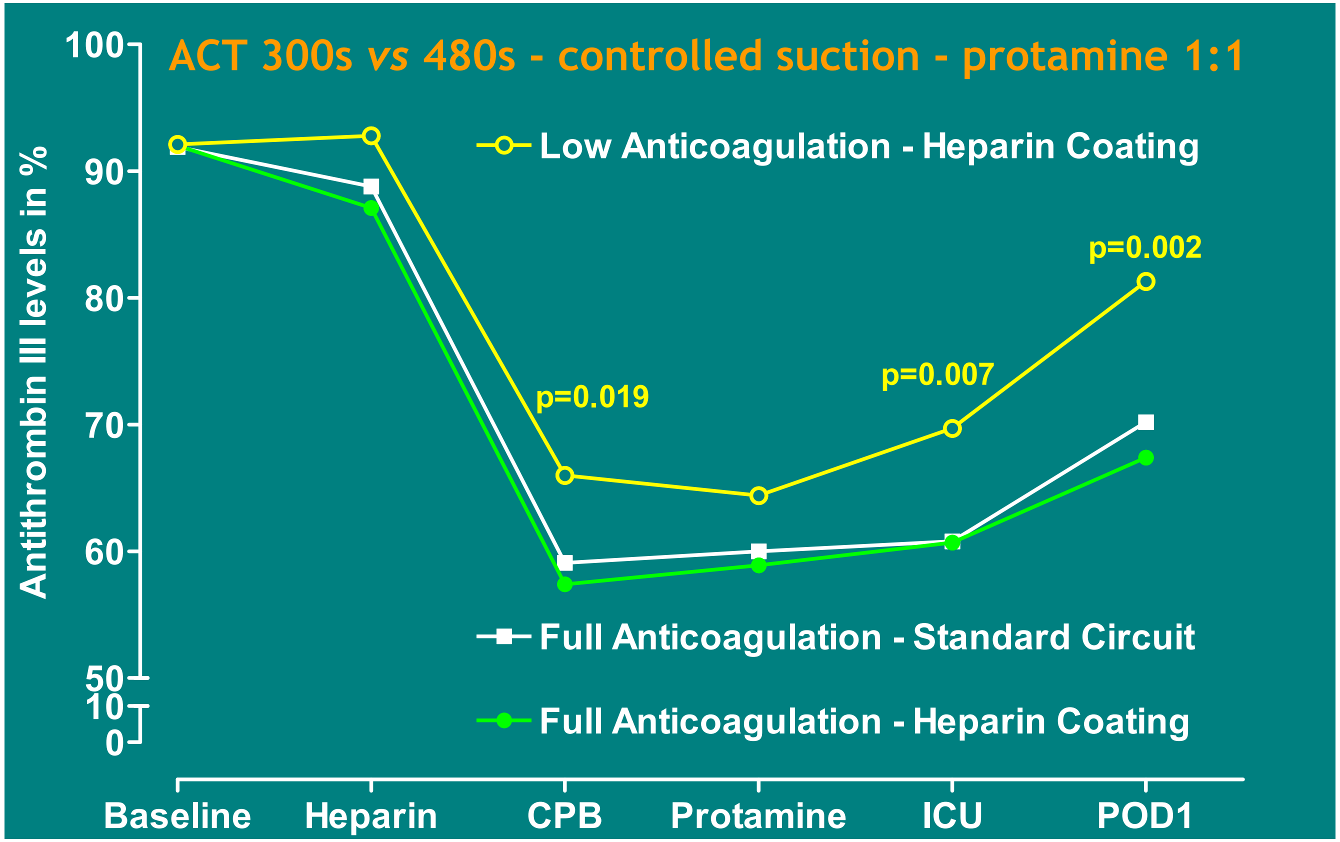
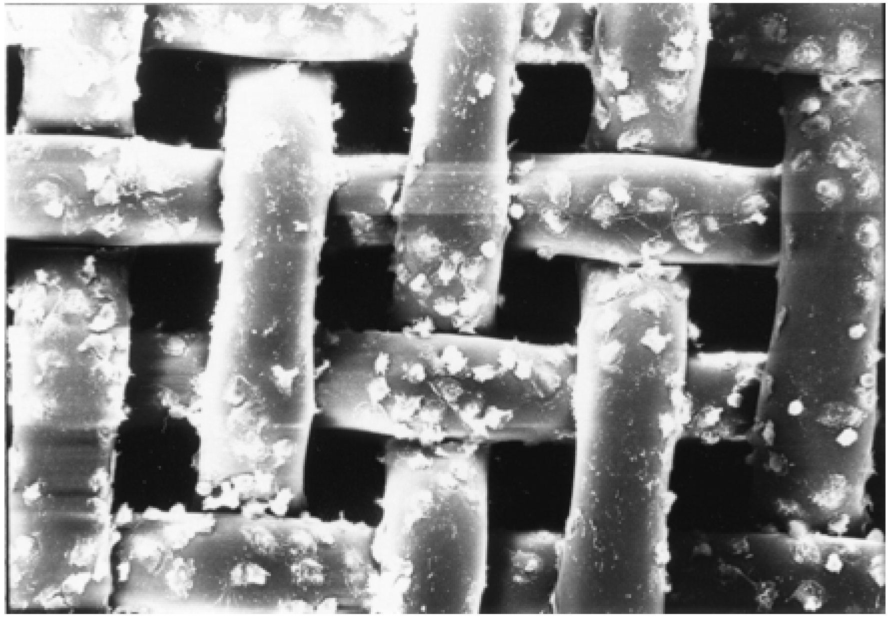
Préservation des concentrations d'antithrombine après CEC en réduction d'anticoagulation



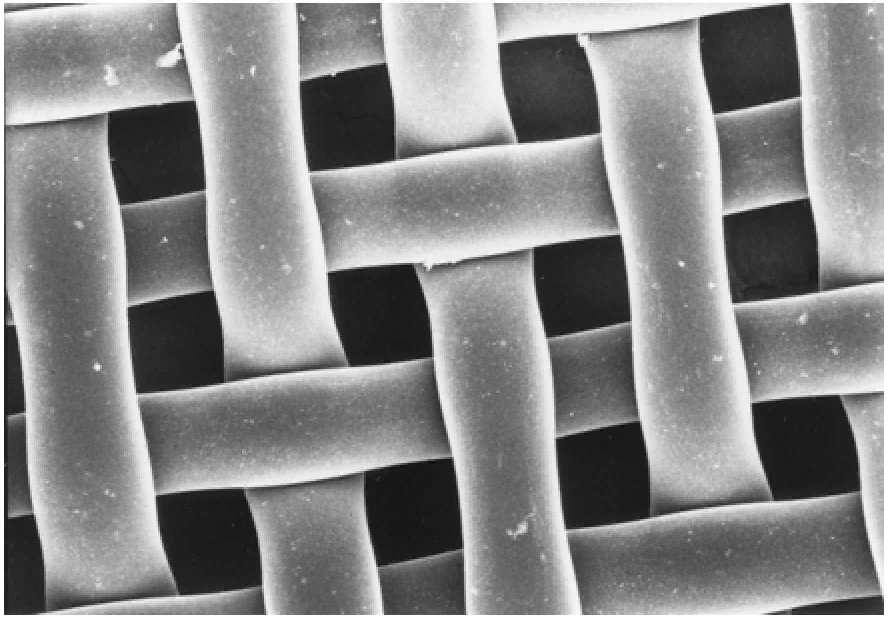
Ranucci M, et al. The Antithrombin III-Saving Effect of Reduced Systemic Heparinization and Heparin-Coated Circuits. J Cardiothorac Vasc Anesth 2002;16(3):316–20.

Réduction d'anticoagulation et dépôts cellulaires sur les surfaces artificielles

Microscopie électronique à balayage x350



Heparin-coated ECC
Full heparinization
300 IU/Kg ACT > 400 s.



Heparin-coated ECC
Reduced heparinization
200 IU/Kg ACT > 300 s.

Nakajima T, et al. Reduction of heparin dose is not beneficial to platelet function. Ann Thorac Surg 2000;70(1):186–90.

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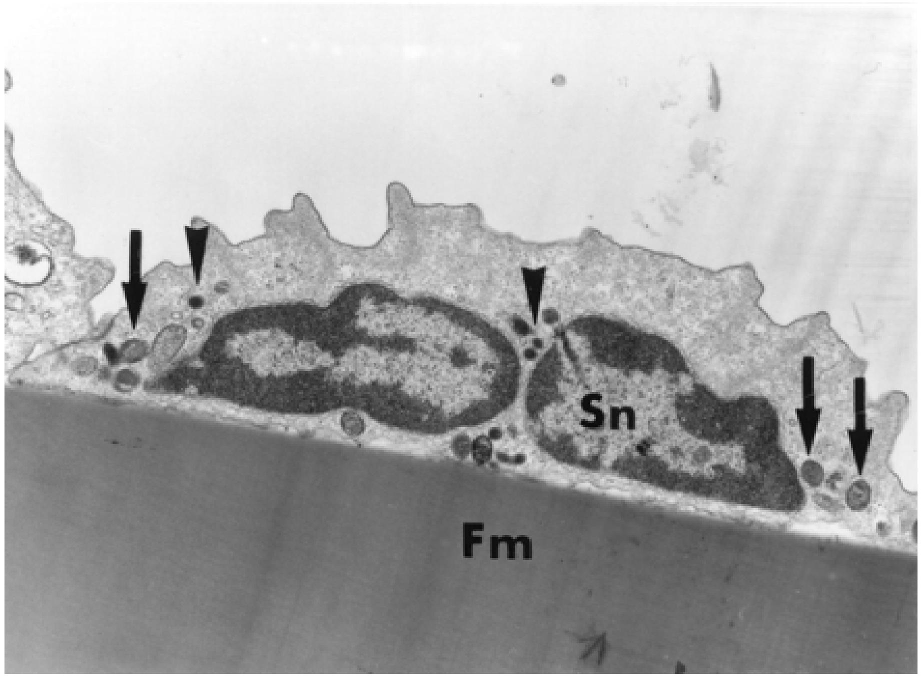
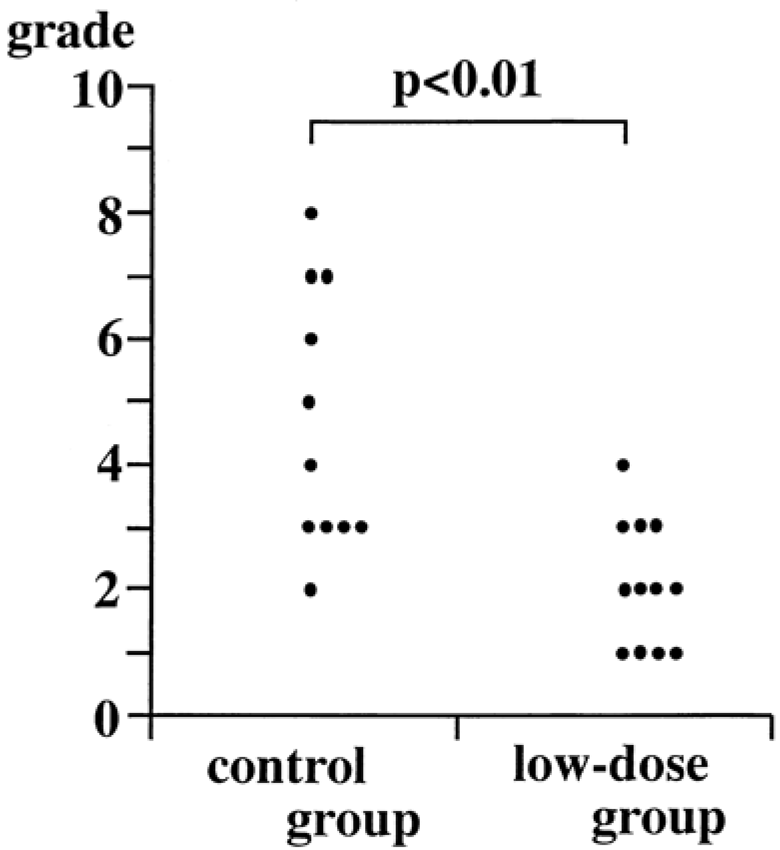
Réduction d'anticoagulation et dépôts cellulaires sur les surfaces artificielles

Microscopie électronique à transmission x 7500





Adhésion leucocytaire

Nakajima T, et al. Reduction of heparin dose is not beneficial to platelet function. Ann Thorac Surg 2000;70(1):186-90.

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Impact de l'héparine sur l'activation endothéliale en chirurgie à cœur ouvert

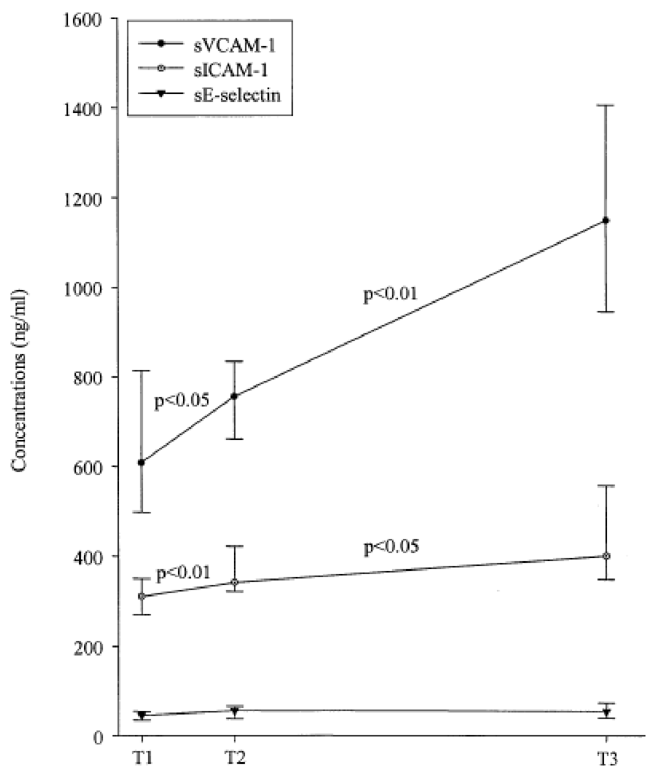

Fig 1. Concentrations of sVCAM-1, sICAM-1, and sE-selectin (median ± 95% confidence interval) in sera from patients undergoing open heart surgery (n = 21). Sampling times: T1 = before anesthesia, T2 = after retransfusion of blood from the heart-lung machine, and T3 = the first postoperative morning. The p values refer to differences between subsequent time points.

The higher heparin dose, the higher endothelial activation

Variable	Significant Variables	*p* Value	Coefficient
sICAM-1 at T2	Age	0.012	−6.174
sICAM-1 at T3	Age	0.034	−0.329
sVCAM-1 at T2	Heparin dose	0.005	0.003
...	Protamine dose	0.007	−0.002
sVCAM-1 at T3	Aortic cross-clamping time	0.037	0.009
sE-selectin at T2	Heparin dose	0.002	0.179
sE-selectin at T3	Age	0.005	−2.072
...	Heparin dose	0.003	0.185
...	Protamine dose	0.060	0.164

Eikemo H, Sellevold OFM, Videm V. Markers for endothelial activation during open heart surgery. Ann Thorac Surg. 2004;77(1):214-9.

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Cette approche est elle également fiable et réalisable en chirurgie à cœur ouvert ?

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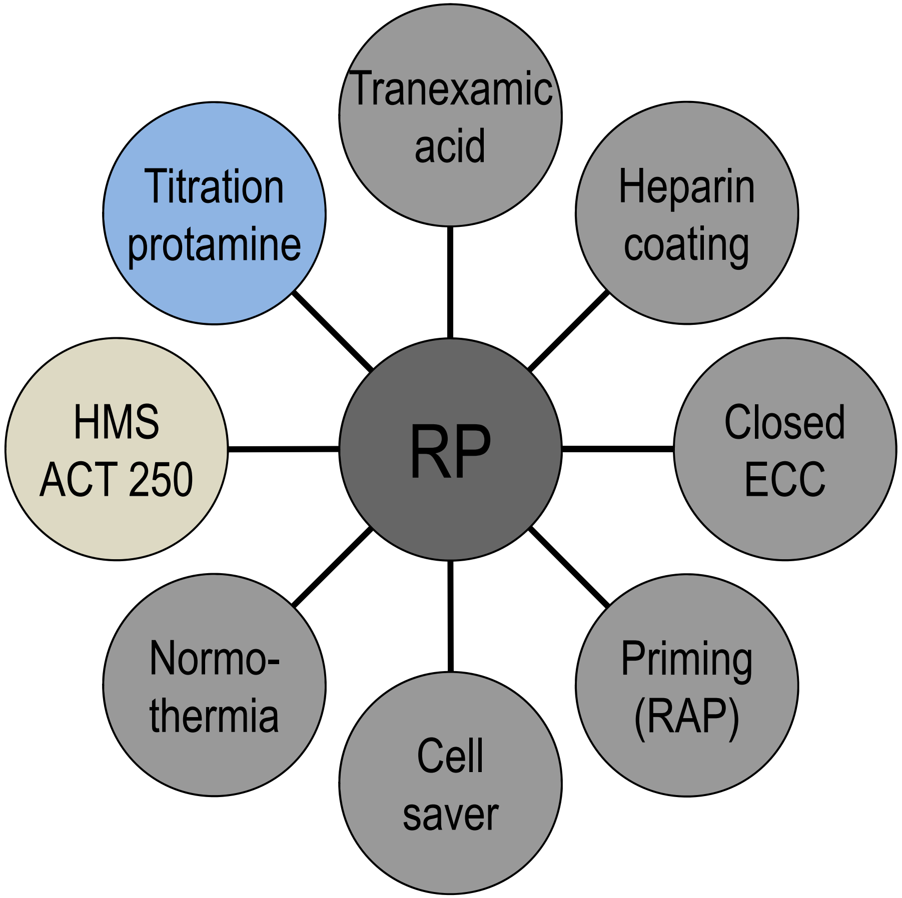
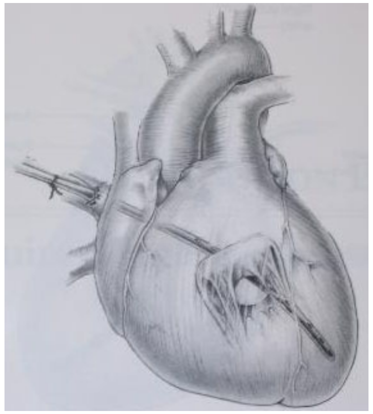
Principes en chirurgie à cœur fermé

Décharge gauche déclive par VPSD

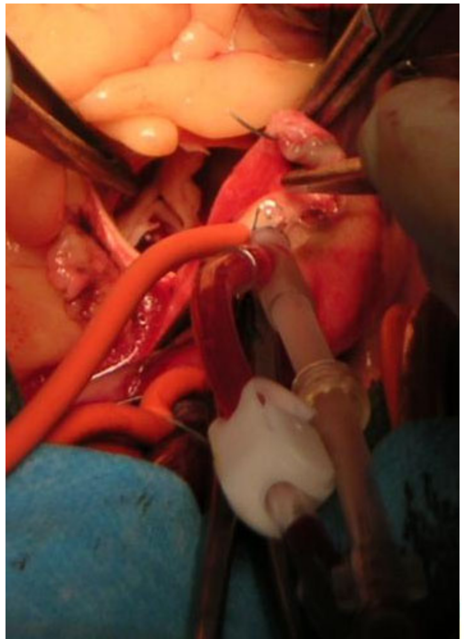




La décharge gauche par déclivité disparaît quand on ouvre les cavités cardiaques

A cœur fermé:

- **Déclivité**
- **Sang toujours en contact de surface hémocompatible**



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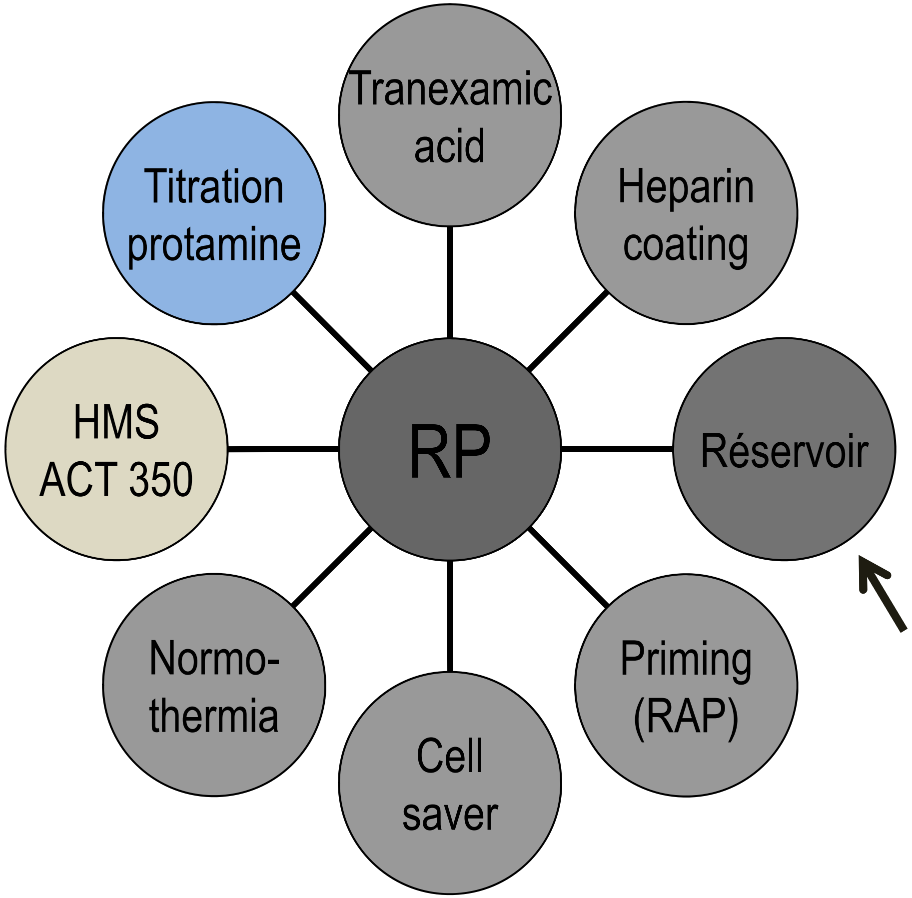
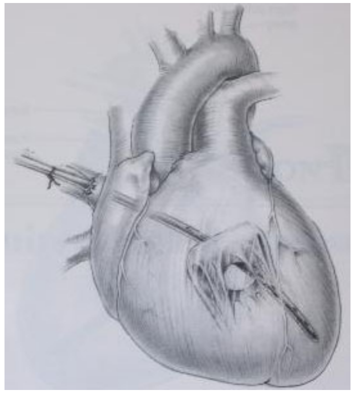
Adaptations en chirurgie à cœur ouvert

Décharge gauche déclive par VPSD

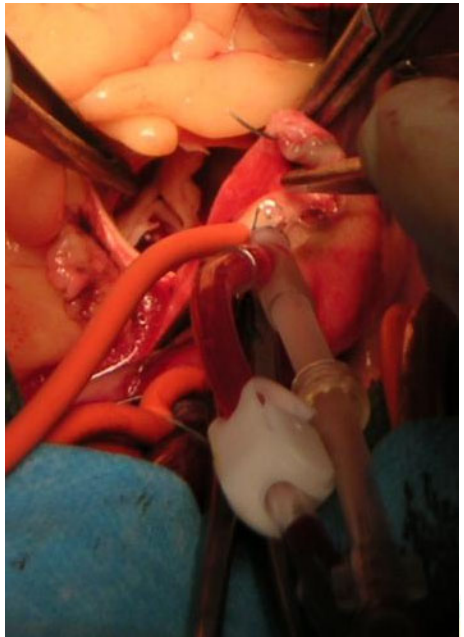




A cœur ouvert (valve)

- **Sang toujours en contact de surface hémocompatible**

La décharge gauche par déclivité disparaît quand on ouvre les cavités cardiaques



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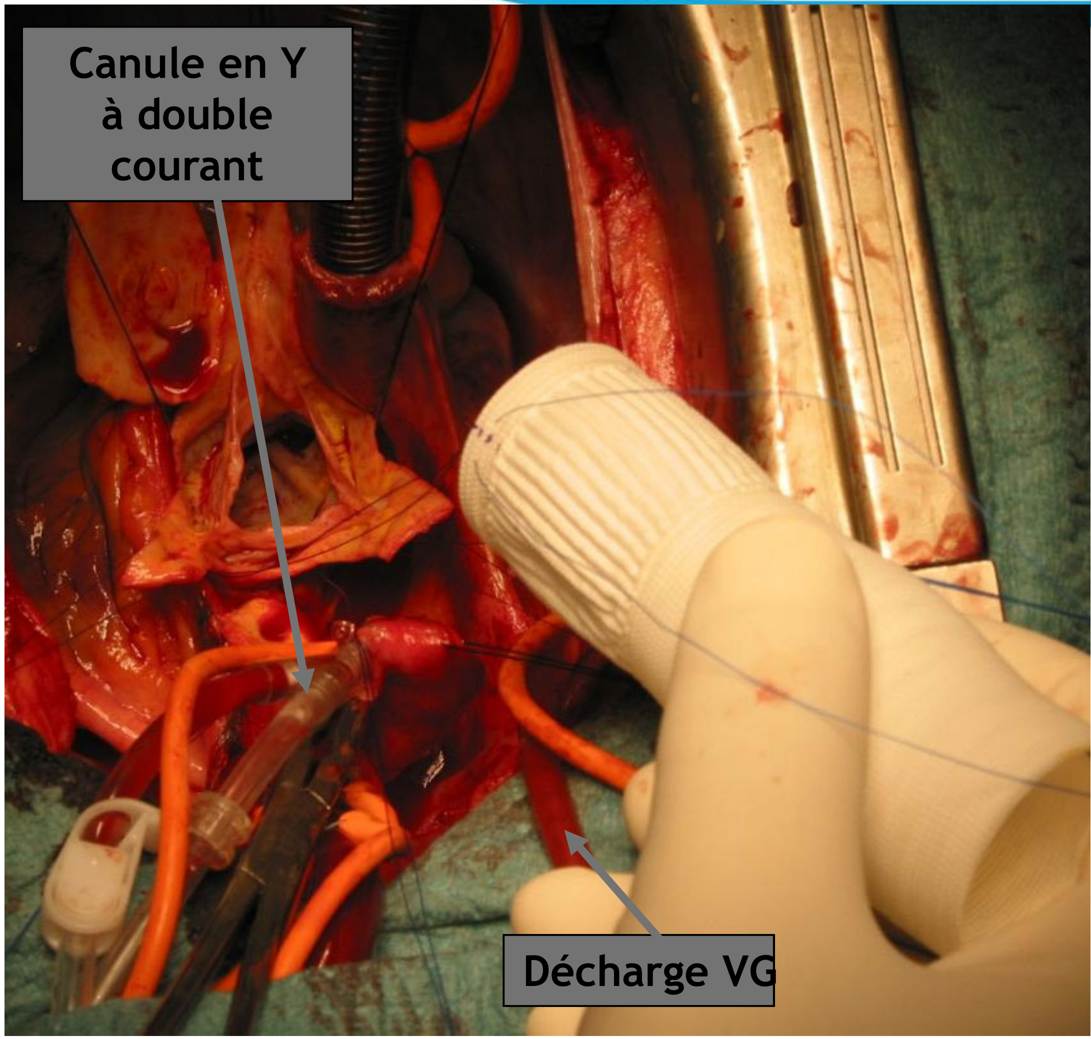
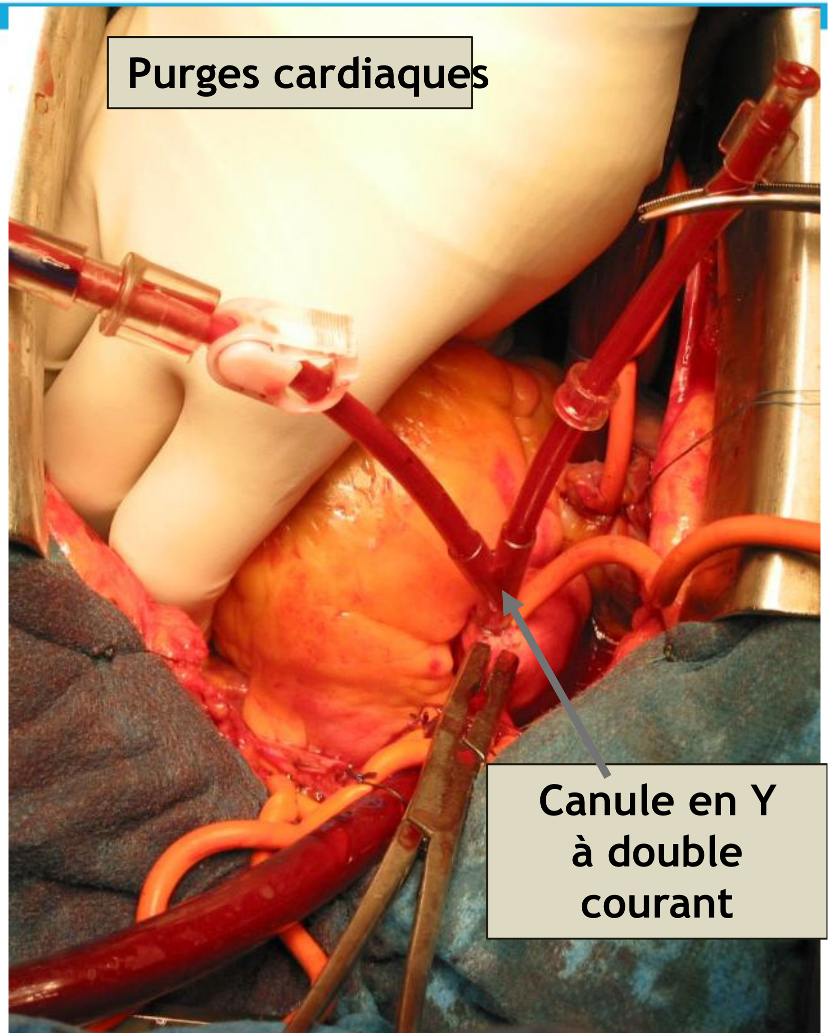
Intervention de Tirone David avec ACT 350 s

Décharge ventriculaire gauche et purges des cavités cardiaques





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Optimisation de la CEC
Guidelines OpECC – MiECC – ERAS (RAAC)

Check for updates

Review

Perfusion

Perfusion
2022, Vol. 0(0) 1–24

DOI: 10.1177/02676591221119002
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2021 MiECTiS focused update on the 2016 position paper for the use of minimal invasive extracorporeal circulation in cardiac surgery

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Guidelines

Guidelines on enhanced recovery after cardiac surgery under cardiopulmonary bypass or off-pump[☆,☆☆]

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☆ Validated by the SFAR Clinical Practice Guidelines Committee on the 10th of May 2021, the SFAR Board of Directors on the 19th of May 2021, and the SFCTCV Board of Directors on the 05th of June 2021.
☆☆ Clinical guidelines issued by the French Society of Anaesthesia and Intensive Care Medicine (Société française d'anesthésie et de réanimation) and the French Society of Thoracic and Cardiovascular Surgery (Société française de chirurgie thoracique et cardio-vasculaire).

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1 The two first authors have contributed equally to the editing process.

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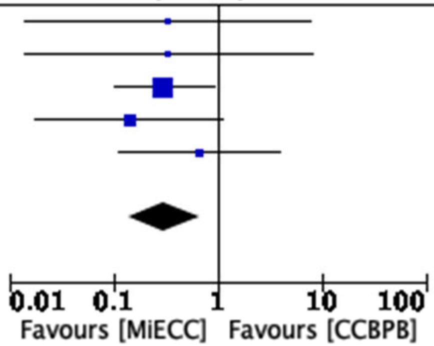
Méta-analyse comparant CEC conventionnelle et optimisée
Infarctus myocardique postopératoire

Study or Subgroup	MiECC Events	MiECC Total	CCPB Events	CCPB Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year	A	B	C	D	E	F	G
Beghi, 2006	0	30	1	30	5.7%	0.33 [0.01, 7.87]	2006	+	+		+			−
Castiglioni 2009	0	60	1	60	5.7%	0.33 [0.01, 8.02]	2009			−				
El-Essawi 2011	4	252	13	248	50.2%	0.30 [0.10, 0.92]	2011	+	+	−	−			
Asteriou 2013	1	100	7	100	26.8%	0.14 [0.02, 1.14]	2013			−				−
Ellam 2020	2	120	3	120	11.5%	0.67 [0.11, 3.92]	2020			−				
Total (95% CI)		562		558	100.0%	0.31 [0.14, 0.67]								
Total events	7		25											

Heterogeneity: $Chi^2 = 1.27$, df = 4 ($P = 0.87$); $I^2 = 0\%$
Test for overall effect: $Z = 2.97$ ($P = 0.003$)

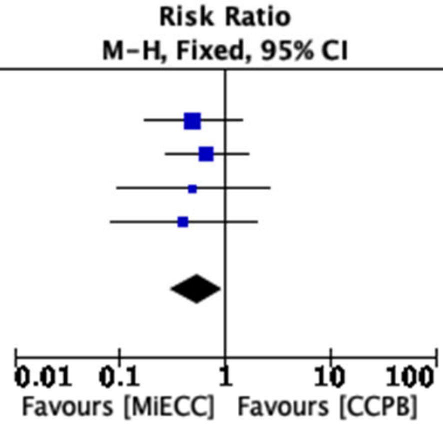


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Méta-analyse comparant CEC conventionnelle et optimisée
Bas débit cardiaque

Study or Subgroup	MiECC Events	MiECC Total	CCPB Events	CCPB Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year	Risk of Bias A	B	C	D	E	F	G
Remadi 2004	1	0	3	0		Not estimable	2004			-	+			
Remadi 2006	5	200	10	200	35.7%	0.50 [0.17, 1.44]	2006			-				
Beghi, 2006	6	30	9	30	32.1%	0.67 [0.27, 1.64]	2006	+	+		+			-
Castiglioni 2009	2	60	4	60	14.3%	0.50 [0.10, 2.63]	2009			-				
Anastasiadis 2013	2	60	5	60	17.9%	0.40 [0.08, 1.98]	2013	+	+	-				-
Total (95% CI)		350		350	100.0%	0.54 [0.30, 0.97]								
Total events	16		31											

Heterogeneity: Chi² = 0.38, df = 3 (P = 0.94); I² = 0%
Test for overall effect: Z = 2.07 (P = 0.04)

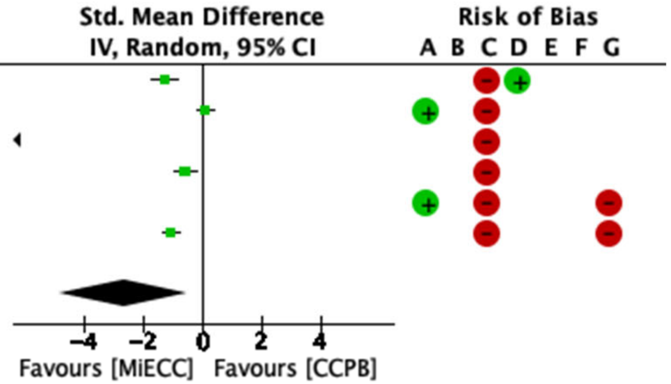


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Libération enzymatique
Souffrance cellulaire myocardique

Study or Subgroup	MiECC Mean	MiECC SD	MiECC Total	CCPB Mean	CCPB SD	CCPB Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Remadi 2004	4.65	2.9	50	9.5	4.4	50	20.0%	−1.29 [−1.72, −0.86]	2004
Abdel-Rahman 2005	13.3	14.9	101	12.1	10.7	103	20.1%	0.09 [−0.18, 0.37]	2005
Remadi 2006	3.4	0.3	200	15	1.5	200	19.7%	−10.70 [−11.47, −9.93]	2006
Castiglioni 2009	3.8	2.7	60	6.63	6.25	49	20.1%	−0.61 [−0.99, −0.22]	2009
Anastasiadis 2010	830	980	50	1,033	828	0		Not estimable	2010
Asteriou 2013	33.6	28.2	100	72.5	41.9	100	20.1%	−1.09 [−1.38, −0.79]	2013
Total (95% CI)			561			502	100.0%	−2.69 [−4.87, −0.50]	

Heterogeneity: $Tau^2 = 6.16$; $Chi^2 = 675.48$, df = 4 ($P < 0.00001$); $I^2 = 99\%$
Test for overall effect: Z = 2.41 (P = 0.02)



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(F) Selective reporting (reporting bias)
(G) Other bias

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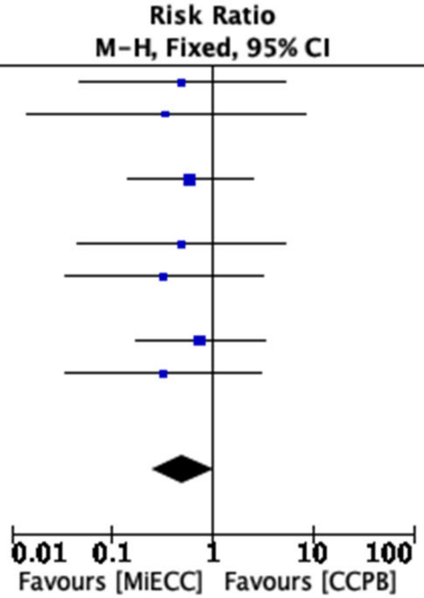
Méta-analyse comparant CEC conventionnelle et optimisée
Mortalité postopératoire

Study or Subgroup	MiECC Events	MiECC Total	CCPB Events	CCPB Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year	A	B	C	D	E	F	G
Remadi 2004	1	50	2	50	9.7%	0.50 [0.05, 5.34]	2004			−	+			
Abdel-Rahman 2005	0	101	1	103	7.2%	0.34 [0.01, 8.25]	2005	+		−				
Beghi, 2006	0	30	0	30		Not estimable	2006	+	+		+			−
Remadi 2006	3	200	5	200	24.3%	0.60 [0.15, 2.48]	2006			−				
Castiglioni 2009	0	60	0	60		Not estimable	2009			−				
Anastasiadis 2010	1	50	2	49	9.8%	0.49 [0.05, 5.23]	2010	+		−				−
El-Essawi 2011	1	252	3	248	14.7%	0.33 [0.03, 3.13]	2011	+	+	−	−			
Anastasiadis 2013	0	60	0	60		Not estimable	2013	+	+	−				−
Asteriou 2013	3	100	4	100	19.5%	0.75 [0.17, 3.27]	2013			−				−
Baumbach 2016	1	101	3	99	14.7%	0.33 [0.03, 3.09]	2016			−				
Ellam 2020	0	120	0	120		Not estimable	2020			−				
Total (95% CI)		1124		1119	100.0%	0.51 [0.24, 1.06]								
Total events	10		20											

Heterogeneity: $Chi^2 = 0.68$, df = 6 (P = 0.99); $I^2 = 0\%$

Test for overall effect: Z = 1.80 (P = 0.07)



Risk of bias legend
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(G) Other bias

RFE SFCTCV-SFAR RAACC

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Les résultats dans notre pratique quotidienne

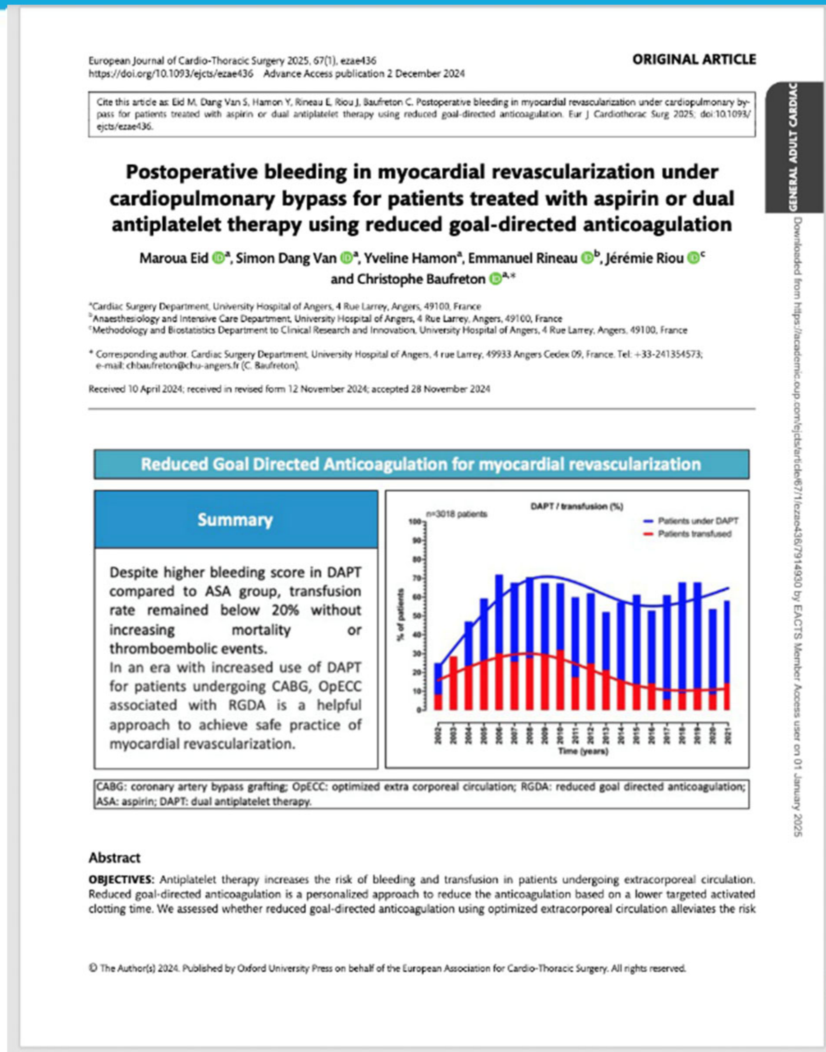
Impact de la réduction

ciblée d'anticoagulation

sous CEC optimisée chez les

patients avec double

antiaggrégation plaquettaire



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ORIGINAL ARTICLE

GENERAL ADULT CARDIAC

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Postoperative bleeding in myocardial revascularization under cardiopulmonary bypass for patients treated with aspirin or dual antiplatelet therapy using reduced goal-directed anticoagulation

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Reduced Goal Directed Anticoagulation for myocardial revascularization

Summary

Despite higher bleeding score in DAPT compared to ASA group, transfusion rate remained below 20% without increasing mortality or thromboembolic events.
In an era with increased use of DAPT for patients undergoing CABG, OpECC associated with RGDA is a helpful approach to achieve safe practice of myocardial revascularization.

CABG: coronary artery bypass grafting; OpECC: optimized extra corporeal circulation; RGDA: reduced goal directed anticoagulation; ASA: aspirin; DAPT: dual antiplatelet therapy.

Abstract

OBJECTIVES: Antiplatelet therapy increases the risk of bleeding and transfusion in patients undergoing extracorporeal circulation. Reduced goal-directed anticoagulation is a personalized approach to reduce the anticoagulation based on a lower targeted activated clotting time. We assessed whether reduced goal-directed anticoagulation using optimized extracorporeal circulation alleviates the risk

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Les résultats dans notre pratique quotidienne

Introduction | Matériel et méthodes | Résultats | Discussion | Conclusion

Objectif de l'étude

ACT cible : 250 sec

CEC biocompatible

Coronaropathies ischémiques isolées

Poursuite des anti agrégants plaquettaires

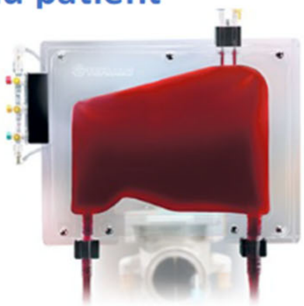
Evaluation des pratiques

Etude du saignement et recours à la transfusion

- SAPT *Single Anti platelet therapy*
- DAPT *Dual Anti platelet therapy*

Les résultats dans notre pratique quotidienne

Gestion per et post opératoire immédiate du patient



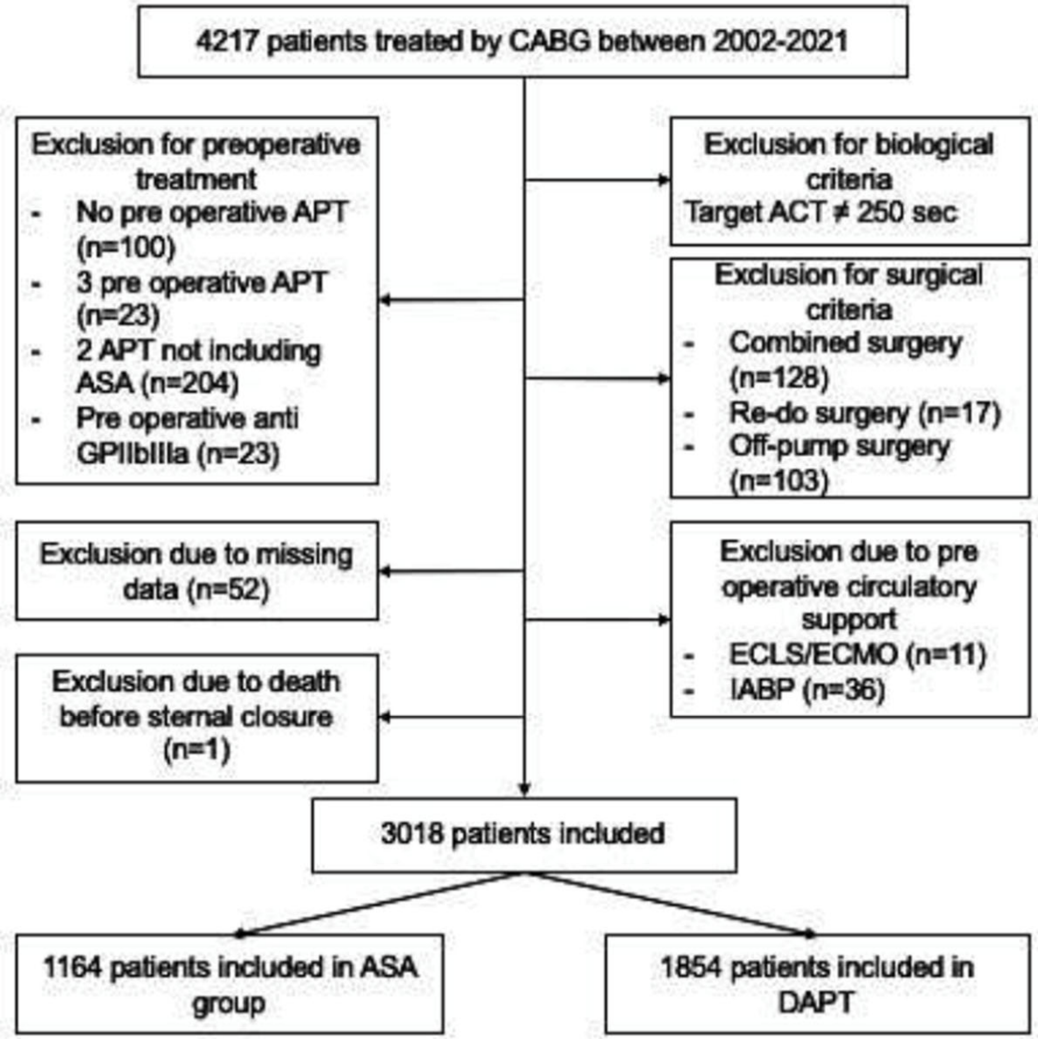
- CEC biocompatible
  - Circuit biocompatible/clos
  - Limitation de l'hémodiluton
  - Normothermie
  - Gestion des aspirations

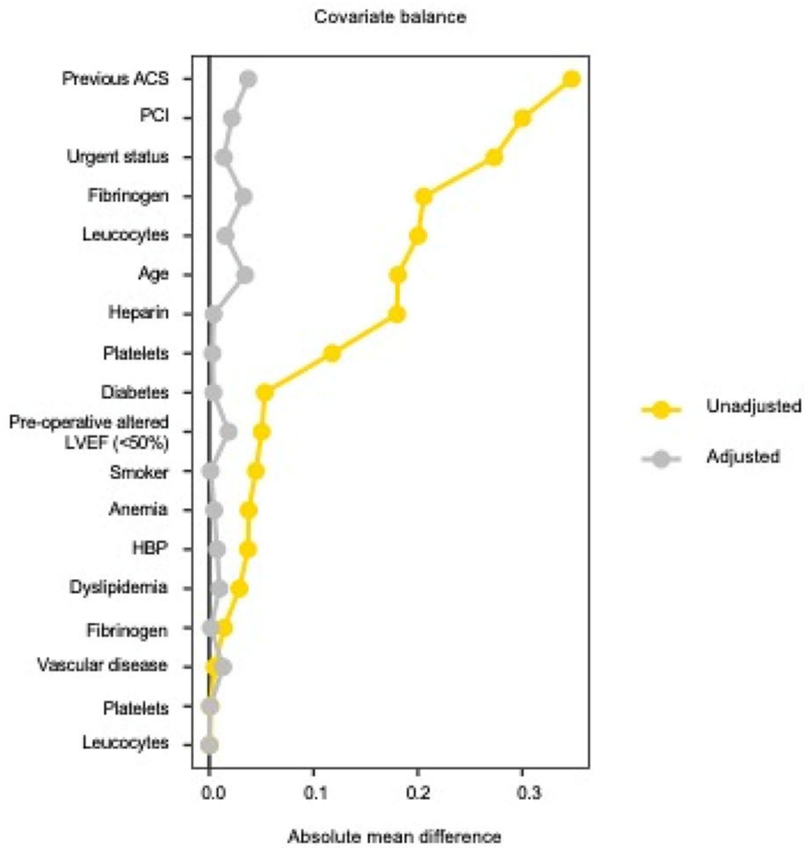
- Suivi de l'anticoagulation per CEC : Hepcon-HMS PLUS® (MEDTRONIC)
  - ACT cible 250 secondes
  - Protaminothérapie adaptée à chaque patient

- Réanimation
  - Cut-off transfusionnels définis
  - Reprise précoce pour hémostase

Baufreton, C. *et al.* *Perfusion* (2002)

Les résultats dans notre pratique quotidienne
Flowchart et score de propension





Ticagrelor < 3 j
Clopidogrel < 5 j
Prasugrel < 7 j

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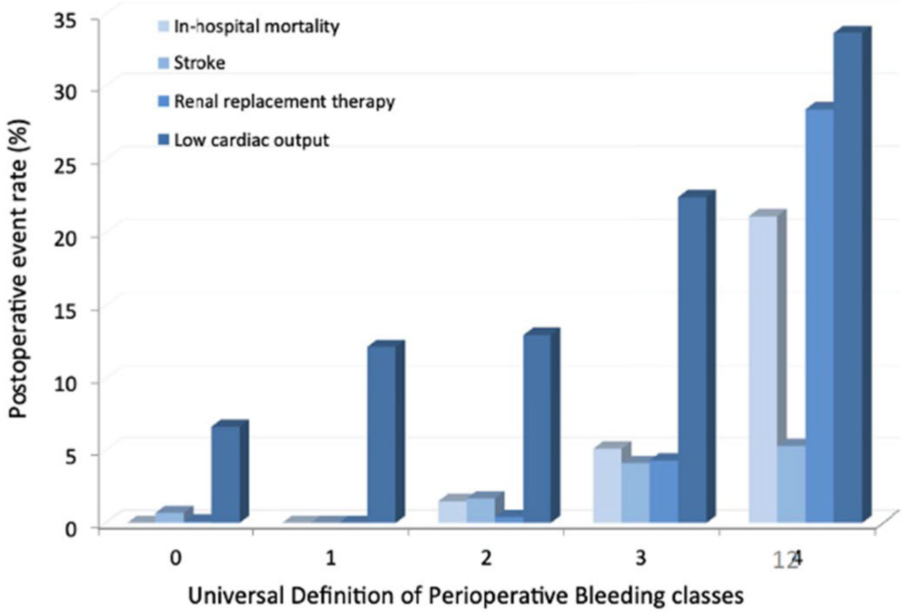
Les résultats dans notre pratique quotidienne
Scores UDPB et E-CABG

Bleeding definition	Sternal closure delayed	Postoperative chest tube blood loss within 12 hours (mL)	PRBC (units)	FFP (units)	PLT (units)	Cryoprecipitate	PCCs	rFVIIa	Reexploration/ tamponade
Class 0 (insignificant)	No	<600	0*	0	0	No	No	No	No
Class 1 (mild)	No	601-800	1	0	0	No	No	No	No
Class 2 (moderate)	No	801-1000	2-4	2-4	Yes	Yes	Yes	No	No
Class 3 (severe)	Yes	1001-2000	5-10	5-10	N/A	N/A	N/A	No	Yes
Class 4 (massive)	N/A	>2000	>10	>10	N/A	N/A	N/A	Yes	N/A

Dyke C, Aronson S, Dietrich W, Hofmann A, Karkouti K, Levi M, et al. Universal definition of perioperative bleeding in adult cardiac surgery. The Journal of Thoracic and Cardiovascular Surgery. 2014 May;147(5):1458-1463.e1.



Kinnunen EM et al. The Journal of Thoracic and Cardiovascular Surgery. 2014 Oct;148(4):1640-1646.e2.

- E-CABG

Grades	*Intervention for treatment of bleeding*	*Additive score*
Grade 0		
	No transfusion of blood products with the exception of 1 unit of RBCs	0
Grade 1		
	Transfusion of platelets	2
	Transfusion of fresh frozen plasma or Octaplas	3
	Transfusion of 2–4 units of RBC	3
Grade 2		
	Transfusion of 5–10 units of RBC	5
	Reoperation for bleeding	5
Grade 3		
	Transfusion of > 10 units of RBC	7

Biancari, F. *et al. J. Cardiothorac. Surg.* (2015)

Les résultats dans notre pratique quotidienne
Score BARC-4
Bleeding Academic Research Consortium

Special Report

Standardized Bleeding Definitions for Cardiovascular Clinical Trials

A Consensus Report From the Bleeding Academic Research Consortium

Roxana Mehran, MD; Sunil V. Rao, MD; Deepak L. Bhatt, MD, MPH; C. Michael Gibson, MS, MD; Adriano Caixeta, MD, PhD; John Eikelboom, MD, MBBS; Sanjay Kaul, MD; Stephen D. Wiviott, MD; Venu Menon, MD; Eugenia Nikolsky, MD, PhD; Victor Serebruany, MD, PhD; Marco Valgimigli, MD, PhD; Pascal Vranckx, MD; David Taggart, MD, PhD; Joseph F. Sabik, MD; Donald E. Cutlip, MD; Mitchell W. Krucoff, MD; E. Magnus Ohman, MD; Philippe Gabriel Steg, MD; Harvey White, MB, ChB, DSc

Advances in antithrombotic therapy, along with an early invasive strategy, have reduced the incidence of recurrent ischemic events and death in patients with acute coronary syndromes (ACS; unstable angina, non–ST-segment–elevation myocardial infarction [MI], and ST-segment–elevation MI).[1–4] However, the combination of multiple pharmacotherapies, including aspirin, platelet $P2Y_{12}$ inhibitors, heparin plus glycoprotein IIb/IIIa inhibitors, direct thrombin inhibitors, and the increasing use of invasive procedures, has also been associated with an increased risk of bleeding.

Editorial see p 2664

Bleeding complications have been associated with an increased risk of subsequent adverse outcomes, including MI, stroke, stent thrombosis, and death, in patients with ACS and in those undergoing percutaneous coronary intervention (PCI),[5–10] as well as in the long-term antithrombotic setting.[11,12] Thus, balancing the anti-ischemic benefits against the bleeding risk of antithrombotic agents and interventions is of paramount importance in assessing new therapies and in managing patients. Prior randomized trials comparing antithrombotic agents suggest that a reduction in bleeding events is associated with improved survival.[13,14]

Because prevention of major bleeding may represent an important step in improving outcomes by balancing safety and efficacy in the contemporary treatment of ACS, bleeding events have been systematically identified as a crucial end point for the assessment of the safety of drugs during the course of randomized clinical trials, and are an important aspect of the evaluation of new devices and interventional therapies.[15] Unlike ischemic clinical events (eg, cardiac death, MI, stent thrombosis), for which there is now general consensus on end-point definitions,[16,17] there is substantial heterogeneity among the many bleeding definitions currently in use. Lack of standardization makes it difficult to optimally organize key clinical trial processes such as adjudication, and even more difficult to interpret relative safety comparisons of different antithrombotic agents across studies, or even within a given trial, because results may vary according to the definition(s) used for bleeding. Finally, as reflected by the various terms used to describe bleeding (serious, severe, catastrophic, major, life-threatening, etc), the heterogeneity of definitions may undermine the ability of clinical trials to meaningfully define the balance of safety and efficacy in vascular interventions.

In response to the need to develop, disseminate, and ultimately adopt standardized bleeding end-point definitions for patients receiving antithrombotic therapy, the Bleeding Academic Research Consortium (BARC) convened in February 2010 at the US Food and Drug Administration (FDA) headquarters in White Oak, MD. Modeled after the 2006 Academic Research Consortium, which standardized key ischemic end-point definitions in studies aimed at evaluating coronary stents,[17] the BARC effort brought together representatives from academic research organizations, the FDA, the National Institutes of Health, and pharmaceutical and cardiovascular device manufacturers and independent physician thought leaders in the field of cardiovascular disease to develop consensus bleeding definitions that would be useful

The BARC represents a collaboration of independent academic research organizations (Cardialysis, Rotterdam, the Netherlands; Cardiovascular Research Foundation, New York City, NY; Duke Clinical Research Institute, Durham, NC; TIMI Study Group, Cardiovascular Division, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA; Harvard Clinical Research Institute, Boston, MA; Green Lane Coordinating Centre, Auckland, New Zealand; Cleveland Clinic Coordinating Center for Clinical Research, Cleveland, OH; and PERFUSE, Boston, MA), professional societies (European Society of Cardiology, and Society of Cardiac Angiography and Intervention), federal agencies (the US FDA, National Institutes of Health), and independent expert scientists and consultants (Appendix).

Guest Editor for this article was Frans J. Van de Werf, MD, PhD.

The online-only Data Supplement is available with this article at http://circ.ahajournals.org/cgi/content/full/123/23/2736/DC1.

Correspondence to Roxana Mehran, MD, Mount Sinai Medical Center, One Gustave L. Levy Place, Box 1030, New York, NY 10029. E-mail roxana.mehran@mssm.edu

(*Circulation*. 2011;123:2736-2747.)

Circulation is available at http://circ.ahajournals.org DOI: 10.1161/CIRCULATIONAHA.110.009449

2736

Type 4: CABG-related bleeding

- Perioperative intracranial bleeding within 48h
- Re-operation after closure of sternotomy for the purpose of controlling bleeding
- Transfusion of ≥ 5 U whole blood or packed red blood cells within a 48-h period
- Chest tube output ≥2L within a 24-h period

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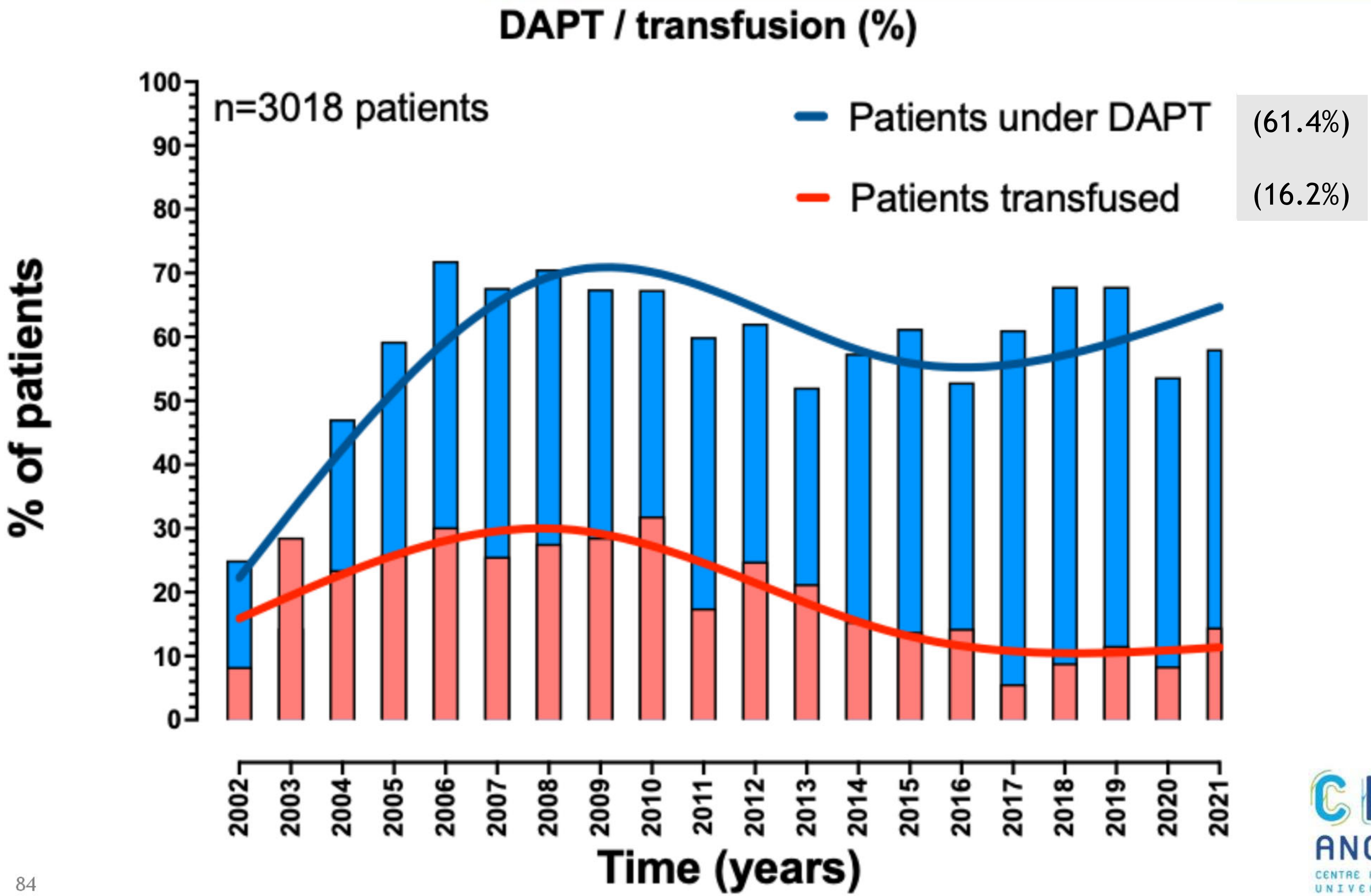
Les résultats dans notre pratique quotidienne
Population globale (n=3018)



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Les résultats dans notre pratique quotidienne

Variable	Propensity-score matched population			
	Overall n=2275	ASA n=1164	DAPT n=1111	p-value
Arterial grafts				
LIMA, n (%)	2259 (99.3)	1156 (99.3)	1103 (99.3)	0.984
BIMA, n (%)	1298 (57)	694 (59.6)	604 (54.3)	0.019
Aortic cross clamp time (min), mean (SD)	63.1 (24)	62.7 (24.5)	63.6 (23.4)	0.408
CPB time (min), mean (SD)	89.8 (30.9)	88.9 (31.4)	90.7 (30.3)	0.213
Total heparin dose delivered (IU), mean (SD)	13960 (5070)	14470 (5190)	13430 (4880)	<0.0001
Total protamine dose delivered (mg), mean (SD)	67.5 (26.6)	69.6 (26.5)	65.3 (26.4)	0.0004
Baseline ACT before CPB (s), mean (SD)	137.6 (12.4)	137.2 (12.3)	137.9 (12.5)	0.222
Maximum ACT (s) on pump, mean (SD)	322.3 (45.7)	318.7 (43.7)	326.0 (47.4)	0.0006
Minimum ACT (s) on pump, mean (SD)	240.9 (30.1)	239.5 (29.1)	242.4 (31.1)	0.0404
Post-protamine ACT (s), mean (SD)	137.6 (14.1)	136.6 (13.9)	138.7 (14.1)	0.0011

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Les résultats dans notre pratique quotidienne

Variable	Propensity-score matched population			
	Overall n=2275	ASA n=1164	DAPT n=1111	p-value
E-CABG score ≧2, n (%)	94 (4.11)	34 (2.92)	59 (5.31)	0.0065
UDPB score ≧3, n (%)	61 (2.68)	21 (1.8)	40 (3.57)	0.0162
BARC 4, n (%)	96 (4.2)	40 (3.44)	57 (5.09)	0.0626
Reoperation for bleeding, n (%)	75 (3.33)	29 (2.49)	46 (4.18)	0.03
Pleural effusion, n (%)	84 (3.70)	32 (2.75)	51 (4.62)	0.033
Units of RBC transfused, mean (SD)	0.402 (1.3)	0.248 (1.1)	0.56 (1.5)	<0.0001
Units of FFP transfused, mean (SD)	0.071 (0.5)	0.045 (0.5)	0.098 (0.5)	0.021
Units of PLT transfused, mean (SD)	0.016 (0.18)	0.009 (0.18)	0.023 (0.17)	0.08
Overall transfusion, n (%)	349 (15.3)	109 (9.5)	239 (21.5)	<0.0001
Chest tube blood loss volume at 12H (mL), mean (SD)	224 (161.9)	192 (136.4)	258 (178.8)	<0.0001
Chest tube blood loss volume at 24H (mL), mean (SD)	322 (211.3)	284 (187.8)	361 (226.9)	<0.0001
Overall chest tube blood loss volume (mL), mean (SD)	386 (296)	338 (274.8)	435 (309)	<0.0001

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Les résultats dans notre pratique quotidienne

Variable	Propensity-score matched population			
	Overall n=2275	ASA n=1164	DAPT n=1111	p-value
30-days mortality, n (%)	25 (1.09)	11 (0.94)	14 (1.24)	0.497
Death of cardiac cause, n (%)	10 (0.44)	3 (0.26)	7 (0.64)	0.278
Postoperative myocardial infarction, n (%)	6 (0.26)	2 (0.17)	4 (0.34)	0.415
Stroke, n (%)	15 (0.67)	5 (0.43)	10 (0.91)	0.217
TIA, n (%)	9 (0.38)	2 (0.17)	7 (0.6)	0.185
AKI, n (%)	189 (8.3)	75 (6.44)	113 (10.17)	0.0025
Wound infection, n (%)	44 (1.94)	13 (1.11)	31 (2.8)	0.010
Ventilation time >24H, n (%)	71 (3.12)	24 (2.06)	47 (4.2)	0.0061
ICU time (hours), mean (SD)	88.8 (101.1)	86.4 (90.3)	91.3 (111.4)	0.301
Total hospitalization time (days), mean (SD)	10.3 (6.6)	9.8 (5.1)	10.8 (7.8)	0.0069

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Impact du niveau d'ACT
(cohorte totale de 3078 patients)

- Analyses multivariées
- Régression logistique des transfusions (tous types)

  → Maximum ACT on pump: *p*-value < 0.001

- Régression linéaire du saignement à H12 postopératoire

  → Maximum ACT on pump: *p*-value < 0.001

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DAPT et saignement/recours à la transfusion
Comparaison au registre E-CABG

	ANGERS (PS matched) (n=2275)	Registre E-CABG* (n=7118)	
DAPT	48,9%	11,6%	(3% à 25%)
Grade E-CABG ≥ 2	5,31%	6,5%	
Grade UDPB ≥ 3	3,57%	8,4%	
Reprise pour saignement	4,18%	2,6%	
Transfusion	21,5%	40,9%	(24,1% à 71,3%)

* Biancari F, Mariscalco G, Gherli R, Reichart D, Onorati F, Faggian G, et al. Variation in preoperative antithrombotic strategy, severe bleeding, and use of blood products in coronary artery bypass grafting: results from the multicentre E-CABG registry. European Hear J - Qual Care Clin Outcomes 2018;4:246–57.

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Comparaison avec EBM
Impact de la RGDA

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https://doi.org/10.1093/ejcts/ezae265 Advance Access publication 5 July 2024

META-ANALYSIS

MYOCARDIAL REVASCULARIZATION

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Platelet inhibitor withdrawal and outcomes after coronary artery surgery: an individual patient data meta-analysis

Michael Schoerghuber[a], Thomas Kuenzer[b], Fausto Biancari[c], Magnus Dalén[d,e], Emma C. Hansson[f,g], Anders Jeppsson[f,g], Georg Schlachtenberger[h], Martin Siegemund[i,j], Andreas Voetsch[k], Gudrun Pregartner[b], Ines Lindenau[l], Daniel Zimpfer[m], Andrea Berghold[b,*], Elisabeth Mahla[a] and Andreas Zirlik[n]

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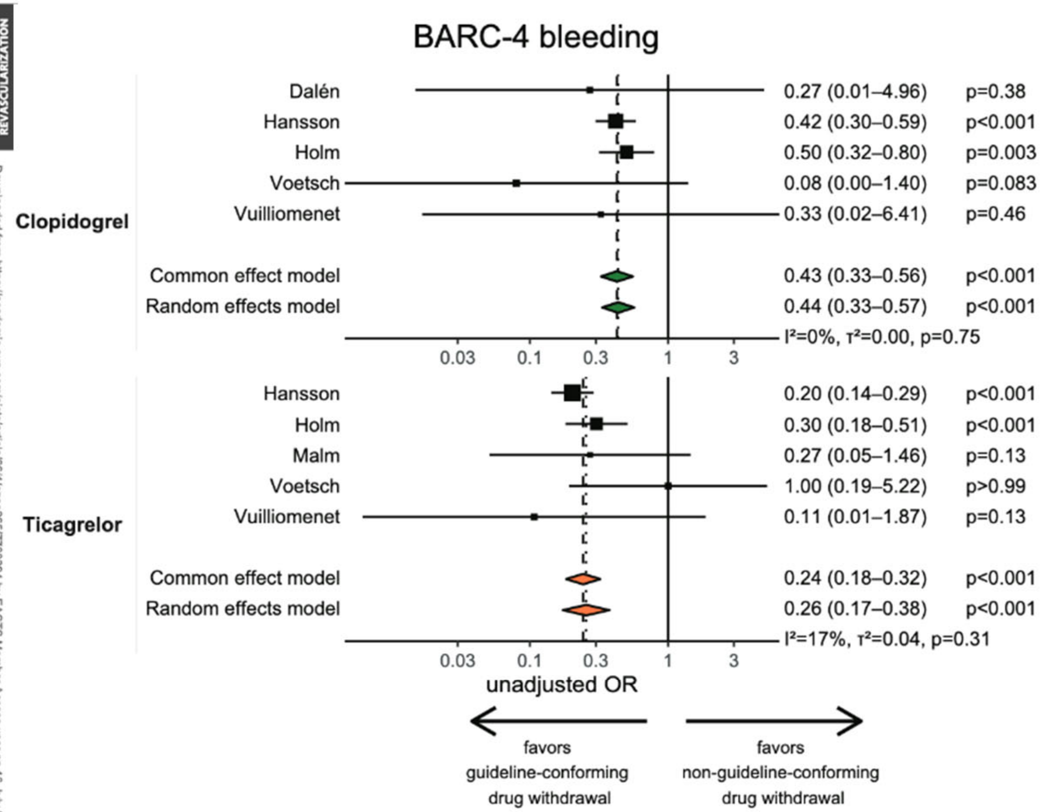
Platelet inhibitor withdrawal and outcomes after coronary artery surgery: an individual patient data meta-analysis

Summary

Individual Patient Data Meta-analysis of 4,837 patients (7 studies) Preoperative guideline-conforming withdrawal of $P2Y_{12}$ receptor inhibitors is associated with a 50% lower BARC-4 bleeding risk in patients undergoing on-pump CABG even after adjusting for EuroSCORE II and cardiopulmonary bypass time.

BARC = Bleeding Academic Research Consortium; CABG = coronary artery bypass grafting; OR = odds ratio.



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Comparaison avec EBM
Impact de la RGDA

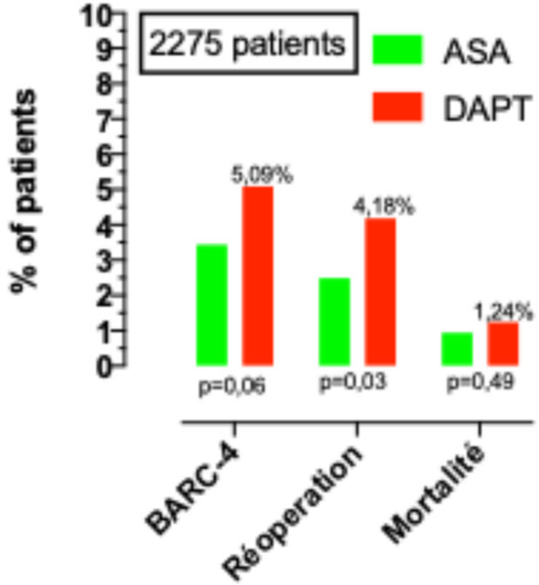
Table 2: Outcome variables according to type of $P2Y_{12}$ receptor inhibitor and drug-specific withdrawal time

Characteristic	Clopidogrel		Ticagrelor		Prasugrel
	<5 days (N = 1391)	≥5 days (N = 1007)	<3 days (N = 644)	≥3 days (N = 1656)	N = 139
BARC-4 bleeding	460 (33%)	99 (9.9%)	214 (33%)	135 (8.2%)	58 (42%)
RBC ≥5 units in 48 h	307 (22%)	77 (7.7%)	166 (27%)	83 (5.1%)	40 (29%)
24-h Chest tube drainage ≥2000 ml	118 (8.6%)	16 (1.6%)	43 (7.1%)	32 (2.0%)	21 (15%)
Reoperation	125 (9.0%)	45 (4.5%)	62 (9.6%)	68 (4.1%)	10 (7.2%)
Intracranial bleeding	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
30-day mortality	41 (4.0%)	11 (1.1%)	33 (6.5%)	18 (1.1%)	6 (7.9%)
Postoperative ischaemic events	93 (8.7%)	28 (2.8%)	53 (9.1%)	46 (2.8%)	10 (9.2%)

BARC-4: Bleeding Academic Research Consortium type 4.

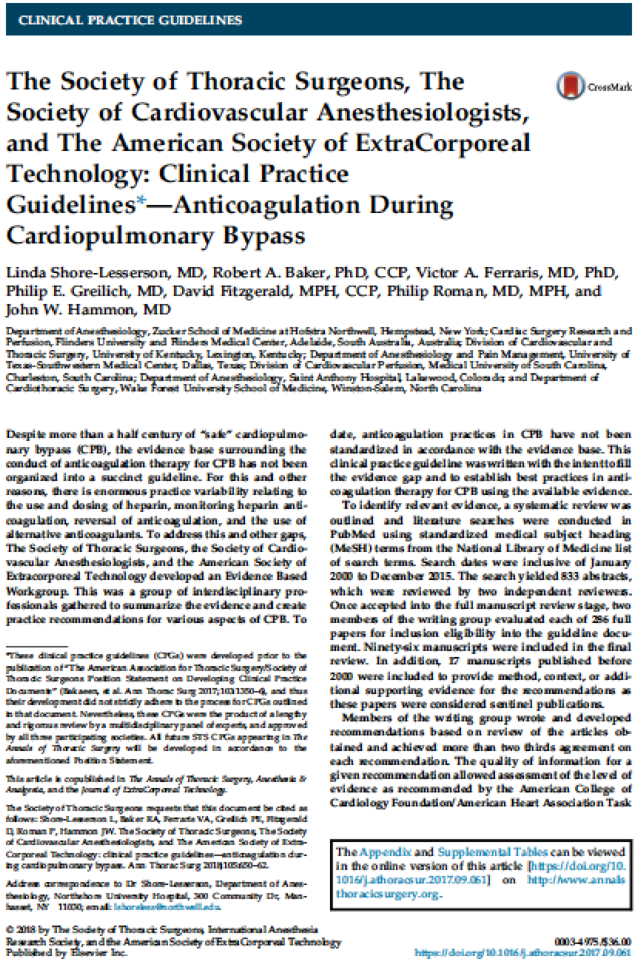
Type 4: CABG-related bleeding

- Perioperative intracranial bleeding within 48 h
- Reoperation after closure of sternotomy for the purpose of controlling bleeding
- Transfusion of ≥5 U whole blood or packed red blood cells within a 48-h period†
- Chest tube output ≥2L within a 24-h period



Shore-Lesserson L, et al. The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: Clinical Practice Guidelines—Anticoagulation During Cardiopulmonary Bypass. Ann Thorac Surg. 2018 Feb;105(2):650–62.

2018



CLINICAL PRACTICE GUIDELINES

The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: Clinical Practice Guidelines*—Anticoagulation During Cardiopulmonary Bypass

Linda Shore-Lesserson, MD, Robert A. Baker, PhD, CCP, Victor A. Ferraris, MD, PhD, Philip E. Greilich, MD, David Fitzgerald, MPH, CCP, Philip Roman, MD, MPH, and John W. Hammon, MD

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Despite more than a half century of "safe" cardiopulmonary bypass (CPB), the evidence base surrounding the conduct of anticoagulation therapy for CPB has not been organized into a succinct guideline. For this and other reasons, there is enormous practice variability relating to the use and dosing of heparin, monitoring heparin anticoagulation, reversal of anticoagulation, and the use of alternative anticoagulants. To address this and other gaps, The Society of Thoracic Surgeons, the Society of Cardiovascular Anesthesiologists, and the American Society of Extracorporeal Technology developed an Evidence Based Workgroup. This was a group of interdisciplinary professionals gathered to summarize the evidence and create practice recommendations for various aspects of CPB. To date, anticoagulation practices in CPB have not been standardized in accordance with the evidence base. This clinical practice guideline was written with the intent to fill the evidence gap and to establish best practices in anticoagulation therapy for CPB using the available evidence.

To identify relevant evidence, a systematic review was outlined and literature searches were conducted in PubMed using standardized medical subject heading (MeSH) terms from the National Library of Medicine list of search terms. Search dates were inclusive of January 2000 to December 2015. The search yielded 833 abstracts, which were reviewed by two independent reviewers. Once accepted into the full manuscript review stage, two members of the writing group evaluated each of 286 full papers for inclusion eligibility into the guideline document. Ninety-six manuscripts were included in the final review. In addition, 17 manuscripts published before 2000 were included to provide method, context, or additional supporting evidence for the recommendations as these papers were considered sentinel publications.

Members of the writing group wrote and developed recommendations based on review of the articles obtained and achieved more than two thirds agreement on each recommendation. The quality of information for a given recommendation allowed assessment of the level of evidence as recommended by the American College of Cardiology Foundation/American Heart Association Task

*These clinical practice guidelines (CPGs) were developed prior to the publication of "The American Association for Thoracic Surgery/Society of Thoracic Surgeons Position Statement on Developing Clinical Practice Documents" (Bakaeen, et al. Ann Thorac Surg 2017;103:1350–6), and thus their development did not strictly adhere to the process for CPGs outlined in that document. Nevertheless, these CPGs were the product of a lengthy and rigorous review by a multidisciplinary panel of experts, and approved by all three participating societies. All future STS CPGs appearing in *The Annals of Thoracic Surgery* will be developed in accordance to the aforementioned Position Statement.

This article is copublished in *The Annals of Thoracic Surgery, Anesthesia & Analgesia*, and the *Journal of ExtraCorporeal Technology*.

The Society of Thoracic Surgeons requests that this document be cited as follows: Shore-Lesserson L, Baker RA, Ferraris VA, Greilich PE, Fitzgerald D, Roman P, Hammon JW. The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: clinical practice guidelines—anticoagulation during cardiopulmonary bypass. Ann Thorac Surg 2018;105:650–62.

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The Appendix and Supplemental Tables can be viewed in the online version of this article [https://doi.org/10.1016/j.athoracsur.2017.09.061] on http://www.annalsthoracicsurgery.org.

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https://doi.org/10.1016/j.athoracsur.2017.09.061

It is reasonable to maintain activated clotting time above 480 seconds during CPB. However, this minimum threshold value is an approximation and may vary based on the bias of the instrument being used (Level of Evidence C)

To maintain a margin of safety above 400 seconds, the minimum acceptable ACT value of approximately 480 seconds became a "standard of care" that was used in numerous future studies and in clinical practice, but was ***based on limited evidence***

Options for calculating the initial heparin bolus include a fixed, weight-based dose, (eg, 300 IU/kg), or use of point-of-care tests that measure the whole blood sensitivity to heparin using an associated dose response.

2019

Recommendations for periprocedural anticoagulation management

Recommendations	Class[a]	Level[b]	Ref[c]
Heparin management			
ACT above 480 s during CPB should be considered in CPB with uncoated equipment and cardiotomy suction. The required target ACT is dependent on the type of equipment used.	IIa	C	
Individualized heparin and protamine management should be considered to reduce postoperative coagulation abnormalities and bleeding complications in cardiac surgery with CPB.	IIa	B	[165, 166, 169]
In the absence of individual heparin dosing tools, it is recommended that ACT tests be performed at regular intervals based on institutional protocols, and heparin doses have to be given accordingly.	I	C	

2024

Recommendation Table 37. **Recommendations for heparin administration**

Recommendations	Class[a]	Level[b]	Ref[c]
Individualized heparin and protamine management should be considered to reduce postoperative coagulation abnormalities and bleeding complications in cardiac surgery with CPB.	IIa	B	[479, 480]
It is recommended that ACT checks be performed at regular intervals based on institutional protocols and that heparin doses be administrated accordingly, especially in the absence of individual heparin dosing services.	I	C	-

[a]Class of recommendation.
[b]Level of evidence.
[c]References.
ACT: activated clotting time; CPB: cardiopulmonary bypass.

Conclusion

Rôle essentiel du chirurgien par la qualité et la pertinence de ses pratiques

Major Bleeding, Transfusions, and Anemia: The Deadly Triad of Cardiac Surgery

Marco Ranucci, MD, FESC, Ekaterina Baryshnikova, BD,
Serenella Castelvecchio, MD, FESC, and Gabriele Pelissero, MD, PhD;
for the Surgical and Clinical Outcome Research (SCORE) Group

EDITORIAL

Blood Transfusion as a Quality Indicator in Cardiac Surgery

Aryeh S. Shander, MD
Lawrence T. Goodnough, MD

In the other study, Bennett-Guerrero et al[5] analyzed data from more than 100 000 patients undergoing coronary artery bypass graft surgery with cardiopulmonary bypass in